MEAN PLATELET VOLUME IN CEREBRO VASCULAR ACCIDENTS

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CERTIFICATE

This is to certify that this dissertation titled **"MEAN PLATELET VOLUME IN CEREBRO VASCULAR ACCIDENTS"** submitted by Dr. G. NAGASUNDAR to the faculty of General Medicine, The Tamilnadu Dr. M.G.R. Medical University, and Chennai in partial fulfillment of the requirement for the award of MD degree Branch I (General Medicine) is a bonafide research work carried out by him under our direct supervision and guidance.

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I, Dr. G. NAGASUNDAR, solemnly declare that the dissertation titled **"MEAN PLATELET VOLUME IN CEREBRO VASCULAR ACCIDENTS"** has been prepared by me.

This is submitted to the Tamil Nadu Dr. M.G.R. Medical University, Chennai, in partial fulfillment of the regulations for the award of MD Degree Branch I (General Medicine).

It was not submitted to the award of any degree/ diploma to any University either in part or in full form previously.

Place : Madurai

Date :

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ABBREVATION IN MASTER CHART

ACA	-	Anterior Cerebral Artery
PCA	-	Posterior Cerebral Artery
MCA	-	Middle Cerebral Artery
VBI	-	Vertebro Basilar Artery
LMW Heparin	-	Low Molecular Weight Heparin
CT Scan	-	Computerized Tomography Scan
MRI	-	Magnetic Resonance Image

ABBREVIATION AND ACRONYMS

CT Scan	-	Computerized Tomography Scan
ECG	-	Electro Cardiogram
EDTA	-	Ethylene Diamine Tetra Acetic acid
HDL	-	High density Lipoprotein
LMW	-	Low Molecular Weight Heparin
LDL	-	Low density Lipoprotein
MCV	-	Mean Corpuscular Volume
MPV	-	Mean Platelet Volume
MRI	-	Magnetic Resonance Image
MRS	-	Modified Rankin Scale
RBC	-	Red Blood cells
WBC	-	White Blood cells

CONTENTS

INTRODUCITON

Stroke is a world wide health problem. It makes an important contribution to morbidity mortality and disability in developed as well as developing countries, like India.

Cerebral thrombosis is the most frequent form of stroke encountered in clinical studies, followed by intracerebral hemorrhage. Subarachnoid hemorrhage and cerebral embolism come next as regards to both mortality and morbidity.

After rupture of an atherosclerotic plaque in the cerebral artery there is platelet adhesion activation and aggregation leading to the formation of a thrombus. Higher the number of reactive platelets higher are the chances for cerebral ischemic strokes.

Bancroft et al (2000) reported that platelet volume is a marker and possibly a determinant of platelet function in that, larger platelets are more reactive than normal sized platelets.

Philip Bath et al (2004) observed an association between increased mean platelet volume and increased occurrence of stroke.

REVIEW OF LITERATURE

The role of platelets in acute myocardial infarction has been appreciated for several decades. Yet the last 5-10 years have seen a dramatic increase in the understanding, development, clinical evaluation and therapeutic application of platelet inhibitor therapy.

Platelets play an essential role in haemostasis, thrombosis and coagulation of blood. These tiny cells previously described as “sponges” (Adelson et al, 1961) are known to engage in a complex repertoire of biochemical and molecular activities designed to prevent haemorrhage.

PLATELET STRUCTURAL AND FUNCTIONAL ANATOMY

Light Microscopy

On Wright-Glemsa stained blood smears, platelets appear as small anucleate, ovoid or round cells, with a pale grayish blue cytoplasm that contains homogeneously distributed purple-red granules.

Dimensions

The volumes of circulating platelets from a single individual are heterogeneous and exhibit a lognormal size distribution; and the platelet volume in a single individual (mean platelet volume, MPV) varies from 7 to 9

femtolitres. (Paulus, 1975; Martin et al, 1982; Stenberg and Levin, 1989; Corash, 1977).

Electron Microscopy and Subcellular Organelles

By scanning electron microscopy, circulating blood platelets appear as flat discs, with smooth contours and rare spiny filopodia. Scanning electron microscopy also reveals random openings of a channel system, the surface connected canalicular system, which invaginates throughout the platelet and is the conduit by which granule contents exocytose after stimulation. Although the platelet is anucleate, transmission electron microscopy reveals a cytoplasm packed with a number of different organelles essential to the maintenance of normal haemostasis.

Glycocalyx

Structure : A glycocalyx, 15 to 20 nm thick, is visualized by transmission electron microscopy and contains glycoproteins, glycolipids, mucopolysaccharides, and adsorbed plasma proteins.

Function : The glycocalyx has a net negative surface charge due to sialic acid residues on the proteins and lipids; the charge is thought to minimize attachment of circulating platelets to each other (Coller, 1984). This structure is rich in carbohydrate moieties of membrane-associated glycoproteins, which serve as receptors to mediate transfer of signals by stimulatory agents. The

glycocalyx interacts with platelet activators to facilitate platelet adhesion and aggregation.

Plasma Membrane

Structure : The platelet plasma membrane is a typical trilaminar membrane with glycoproteins, glycolipids, and cholesterol embedded in a phospholipid bilayer.

Function : The plasma membrane contains sodium and calcium ATPase pumps, which are important for maintaining ionic homeostasis. It has a specialized role in providing a surface for the acceleration of blood coagulation, in that a specific platelet coagulant protein, platelet factor 3, resides in this lipoprotein-rich unit membrane.

Surface-connected Canalicular System

Structure : The surface-connected canalicular system, also called the open canalicular system, weaves throughout the cell cytoplasm in a tortuous fashion.

Function : The functions of the surface connected canalicular system are to provide a route of entry and egress for molecules, an internal reservoir of membrane to facilitate platelet spreading and filopodia formation after adhesion and a storage reservoir for membrane glycoproteins that increase on the platelet surface after activation.

Dense Tubular system

Structure : Unlike the surface-connected canalicular system, the dense tubular system is a closed-channel system consisting of narrow, membrane limited tubules, approximately 400 to 600 A in diameter. It is, infact, residual smooth endoplasmic reticulum from the megakaryocyte.

Function : This channel system is involved in the regulation of intracellular calcium transport because it has been reported to selectively bind, sequester, and release divalent cations after activation. The dense tubular system is also the site of prostaglandin synthesis in platelets.

Cytoskeleton

General Structure : The platelet cytoskeleton contains 30 to 50% of total platelet protein and is made up of three major structural components : an actin microfilament network present throughout the cytoplasm, a micro tubule coil localized at the platelet periphery and a membrane skeleton comprising a network of short actin filaments that underlies the inner surface of the plasma membrane. Although they are distinct structures, interconnections between these elements are present.

Structure and Function of Specific Cytoskeletal Elements

Actin Microfilaments : Twenty to thirty percent of total platelet protein is made up of actin (Pollard, 1990). Actin exists in two forms, G-actin (actin monomers) and F-actin (polymerized actin). In the unstimulated platelet, 30 to

40% of actin is polymerized into filaments; the balance of actin monomers are prevented from polymerizing by proteins such as profilin or thymosin B4 that sequester monomeric actin, or by proteins that cap filaments in the intact cell, such as gelsolin.

Upon platelet activation, the proportion of filamentous actin rapidly increases to 60-70%. Actin monomers polymerize onto filaments at platelet peripheries and bundles of new filaments form to fill developing filopodia.

Microtubules : A circumferential microtubule band that supports the discoid form of the platelet is made up of two nonidentical subunit proteins (alpha and Beta tubulin) associated with microtubule associated proteins (MAPs). The 25 nm diameter microtubule coil lies adjacent to, but does not touch, the plasma membrane.

Microtubules are present primarily in their polymerized form in unstimulated platelets. Platelet activation results in microtubule disassembly, then reassembly; such alterations in the marginal microtubule bundle result in platelet shape changes.

Membrane Skeleton : The short actin filaments of the membrane skeleton, which underlie the inner surface of the plasma membrane, together with the microtubule coil, are thought to help stabilize the platelet discoid shape.

Two major platelet membrane glycoproteins, GP IIb-IIIa and GP Ib-IX are associated with the membrane skeleton.

Granules

Platelets contain four distinct populations of granules: alpha granules, dense bodies, lysosomes, and microperoxisomes. After platelet stimulation by agonists, granules fuse with channels of the surface-connected canalicular system and extrude their contents (White, 1974). Internal contraction is required for this extrusion and ultimate discharge into the surrounding medium.

α - Granules :

Structure : α Granules are the predominant granule type in the platelet. The α granule has been subdivided morphologically into three distinct zones by electron microscopy : an electron- dense nucleoid that occupies the bulk of the granule, a peripheral zone of lower electron density that lies adjacent to the granule membrane and 1 to 6 tubular structures that reside in the electron lucent peripheral zone.

Content : B-thromboglobulin and platelet factor 4 have been localized to the dense nucleoid. Von Willebrand factor is present in the tubular structures of the granule peripheral zone. Thrombospondin, and fibrinogen are present in the granular matrix. Other proteins present in α granules include albumin, immunoglobin G (IgG), fibronectin, platelet derived growth factor, GPIIb-IIIa, Beta amyloid protein precursor, factor V, multimerin, a factor V/Va binding

protein, transforming growth factor β1 and a plasminogen activator similar to tissue plasminogen activator.

Proteins present on the α – granule membrane include P-selectin, GP IIb / IIIa, granule membrane protein – 33 (GMP-33), CD9, platelet – endothelial cell adhesion molecule 1 (PECAM-1) and osteonectin.

Dense Bodies :

Structure : Ultrastructurally, dense granules have a bull's eye appearance. They are the most electron-dense organelles in platelets.

Content : The principal constituents of dense granules are a nonmetabolic pool of adenine nucleotides (adenosine triphosphate and diphosphate, ATP and ADP), PPi, calcium and magnesium and serotonin (5-hydroytryptamine). In addition, dense bodies contain guanosine triphosphate and diphosphate (GTP and GDP). The dense granule membrane contains P – selectin and granulophysin.

Lysosomes :

Structure : Lysosomes are small vesicles of approximately 175 to 200 nm.

Content : Lysosomes are the only platelet granules that contain acid hydrolases. Platelet lysosomes contain a large variety of enzymes, including β hexosaminidase and β glycerophosphatase. Lysosomal membrane glycoprotein

(LIMP-CD63) and lysosomal associated membrane proteins 1 and 2 (LAMP-1 and LAMP-2) become expressed on the plasma membrane after activation.

Microperoxisomes :

Structure : Microperoxisomes are small (90-nm) granules that are relatively few in number in platelets and can be demonstrated only cytochemically.

Content : They are reactive with alkaline diaminobenzidine medium. The enzyme responsible for the cytochemical peroxidase activity in microperoxisomes is catalase.

Coated Vesicles :

Structure : Coated vesicles are 70 to 90 nm organelles

Content : The polyhedral coat on the surface of these vesicles is composed of clathrin. Coated pits and vesicles transfer plasma components to platelet granules (Behnke, 1989).

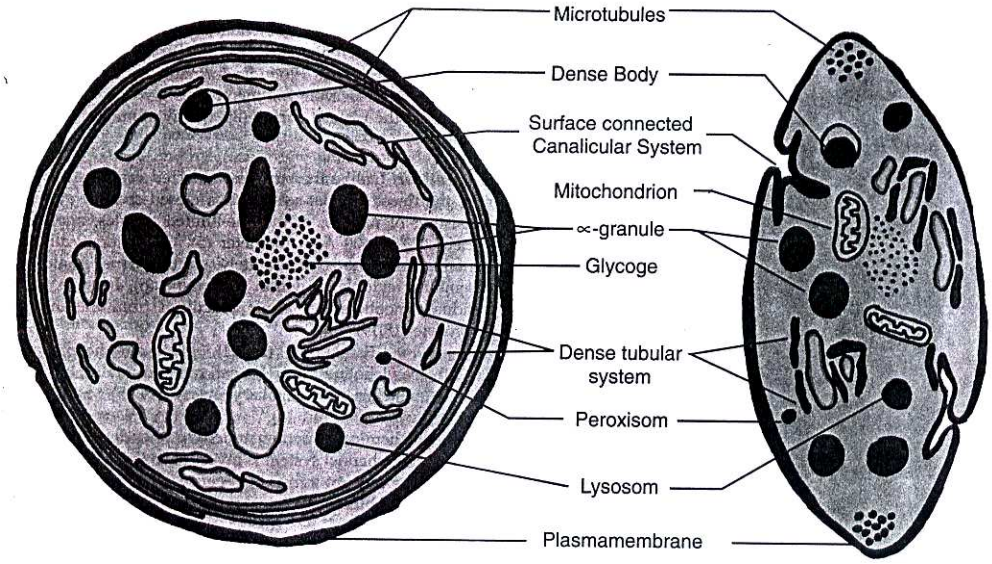
Mitochondria :

Structure : Mitochondria in platelets are similar, with the exception of smaller size to those in other cell types. There are approximately seven per human platelet.

Content : Mitochondria are the site of activity for all components of the respiratory chain and for almost all enzymes in the citric acid cycle.

Glycogen

Platelets contain small particles of glycogen or masses of closely associated glycogen particles; these play an essential role in platelet metabolism.



(Diagram of a human platelet displaying components visible by electron microscopy and cytochemistry)

PLATELET PHYSIOLOGY

Platelet Lipids and Proteins

Membrane Lipids

Phospholipids constitute 80% of the total platelet lipid, although smaller amounts of neutral lipids and glycolipids are also present. The five major phospholipids identified in human platelets are phosphatidylcholine, phosphatidylethanolamine, sphingomyelin, phosphatidylserine and phosphatidylinositol. Almost all platelet fatty acids are esterified in phospholipids, leaving only trace amounts of free fatty acids. Arachidonic acid, the precursor of prostaglandins and thromboxanes, is enriched in these phospholipids and the metabolism of arachidonic acid is critical for normal platelet function (Marcus, 1976).

Neutral lipids make up approximately 28% of total platelet lipids, the predominant neutral lipid being cholesterol.

Membrane Glycoproteins :

Platelet membrane glycoproteins mediate a wide number of adhesive cellular interactions. These glycoproteins function as receptors that can receive signals from outside the platelet, facilitating cell – cell interactions; binding of specific ligands to these receptors results in distinct platelet responses to the external environment.

Glycoprotein IIb / IIIa : Glycoprotein IIb-IIIa is the principal receptor on the platelet plasma membrane (Philips et al, 1988). It is a member of the integrin family of proteins. A Ca2+ dependent conformational change in GP IIb-IIIa after platelet agonist indued stimulation facilitates strong binding to fibrinogen and VWF resulting in cross linking of GP IIb-IIIa molecules on adjacent platelets and platelet aggregation.

Glycoprotein Ib-IX : Glycoprotein Ib mediates the interaction of platelets with VWF. GP Ib also functions as a binding site for thrombin. GP Ib is present on platelet surfaces in a 1:1 ratio with GP IX.

Other membrane Glycoproteins : Membrane glycoproteins GPIa-IIa, GPIc – IIa, mediate platelet adhesion to collagen, fibronectin, laminin and vitronectin. GP V forms a noncovalent complex with GP Ib – IX in the platelet membrane. PECAM-1 binds to heparin like molecules. GPIV is a receptor for thrombospondin. GP IV is also reported to bind collagen.

Other Platelet Proteins : Other proteins presented in the platelet are platelet factor 4, β thromboglobulin, thrombospondin, platelet derived growth factor, fibronectin.

Platelet Factor 4: PF4 binds heparin with high affinity and neutralizes its anticoagulant activity. It exhibits a variety of activities, including the potentiation of platelet aggregation.

PLATELET BIOCHEMISTRY

The platelet has minimal ability to synthesize protein because it contains only low levels of RNA and lacks a nucleus. In terms of dry weight, the platelet is composed of approximately 60% protein, 15% lipid and 8% carbohydrate. Platelet minerals include magnesium, calcium potassium and zinc. Platelets contain substantial amounts of vitamin B12, folic acid, and ascorbic acid.

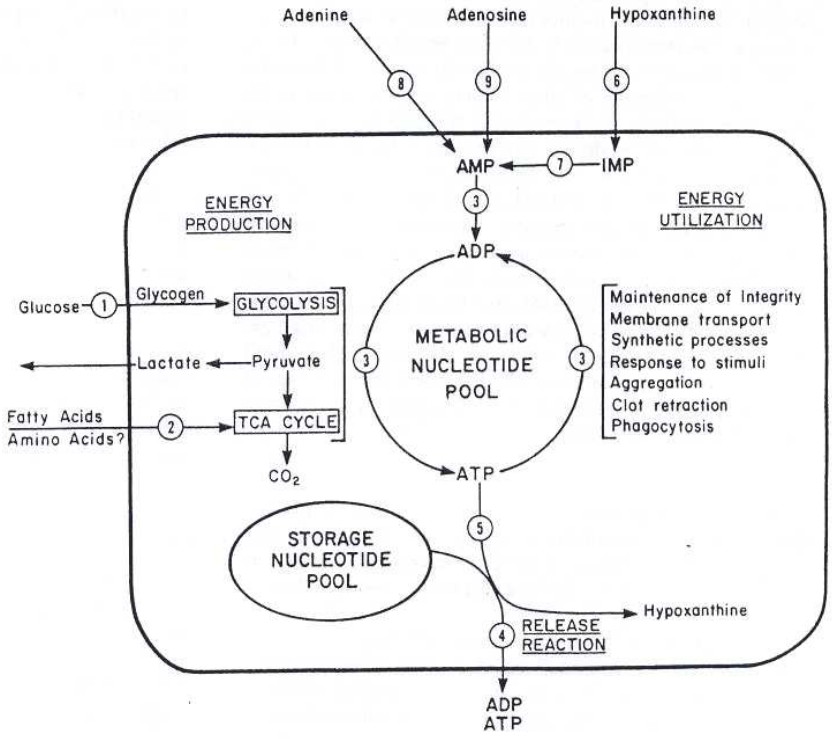
Platelet Energy Metabolism

There are several similarities between the energy metabolism of the platelet and that of skeletal muscle. Both involve active glycolysis and the synthesis and use of large amounts of glycogen and in both, the major mediator of intracellular energy use in an actomyosin-like adenosine triphosphatase. The platelet, like muscle, is metabolically adapted to expend large amounts of energy rapidly during aggregation, the release reaction, and clot retraction.

The major energy source for the platelet is glucose, which is rapidly taken up from the plasma.

A simplified scheme of platelet energy metabolism is shown in the figure below. Platelet energy is derived from the metabolism of glucose and to a lesser extent from the metabolism of fatty acids. Energy is provided in approximately equal amounts by glycolysis and the citric acid cycle. The

platelet energy reserve is provided by the metabolic pool of platelet nucleotides that is in a state of continuous turnover.



(Platelet energy metabolism)

Nucleotide Metabolism

Adenine nucleotides constitute 90% of free platelet nucleotides and are partitioned into at least two different pools, which undergo minimal interchange. The metabolic or cytoplasmic pool makes up 40% of total adenine nucleotides; it is used for the maintenance of various energy-consuming cell functions and is retained during platelet release.

The storage pool, which is present in the dense bodies, contains approximately two-thirds of the total platelet nucleotides, mainly in the form of

ADP and ATP. It is metabolically inactive, does not rapidly incorporate exogenous adenine or phosphate, and equilibrates slowly with the metabolic pool. Nucleotides in this pool are extruded from the platelet during the release reaction and cannot be replenished after release. ATP hydrolysis is required for conversion of G actin to F-actin. The ATP that is broken down to provide energy for the release reaction is not rephosphorylated, but rather is irreversibly degraded to hypoxanthine which diffuses out of the cell. Platelets also contain guanine nucleotides and uracil and cytosine pyrimidines.

Arachidonate Metabolism

Arachidonic acid is released from platelet membrane phospholipids after stimulation by numerous agonists through the enzymatic action of phospholipase A2 or the combination of phospholipase C and diglyceride lipase. After release, arachidonic acid can be acted on by either lipoxygenase, which results in the production of peroxy and hydroxy fatty acids, or by cyclooxygenase, which ultimately results in production of thromboxanes and prostaglandins.

Platelet "Coagulation" Factors

Numerous platelet proteins interact with plasma coagulation proteins although the mechanisms by which platelet membrane component become reorganized and capable of functioning as a catalytic surface for plasma proteins are not known.

Several plasma coagulation factors are associated with platelets, including von Willebrand factor, coagulation inhibitors, and factor XIII.

Various substances associated with or derived from the platelet have been designated platelet factors 1 to 10 and denoted by Arabic numerals. The most important of these are PF4 and PF3.

Platelet Factor 3

PF3 is required in at least two steps in the process of blood coagulation, namely the interaction between factors IXa and VIIIa, which results in the activation of factor X, as well as the interaction between factor Xa and factor Va which leads to the formation of prothrombinase. These coagulation reactions are greatly accelerated on the platelet surface.

PLATELET COUNT

The normal platelet count varies between

1,50,000 – 3,50,000 / mm^3

ORIGIN OF PLATELETS FROM MEGAKARYOCYTES

The megakaryocyte is a large hematopoeitic cell, the cytoplasm of which fragments to form circulating blood platelets. The histogenesis of platelets from megakaryocytes was first described by James Wright in 1910. The megakaryocytes are sessile polyploid cells which inturn descend from diploid pluripotent hematopoeitic stem cells of marrow. The megakaryocytes are imprisoned within the sub endothelial layer of marrow sinuses by their very

girth and volume (average 5000 femtolitres, Zhang YJ, 1991). In these marrow niches, mononuclear progenitors undergo diploid doublings by the unique process of endomitosis. Subsequently the polypoid megakaryocytes accumulate a bulky compartmentalized cytoplasmic mass with large volumes that at end stage maturation disintegrates abruptly to yield between 1000 and 8000 platelets having a volume of 7-9 femto litres each (Martin et al, 1982; Stenberg and Levin, 1989; Corash, 1989). Megakaryocytes are suicidal microorgans whose mission is to proliferate and then fragment their cytoplasm on demand to maintain blood platelets at relatively steady levels of about 1,50,000 – 3,50,000 / mm3.

Maintenance of platelet counts within this range represents a surplus of over 10 times that necessary to ensure routine haemostasis but provides a precautionary reserve for times of excess platelet loss or consumption.

PLATELET LIFE SPAN, TURN OVER & REMOVAL

Platelet life span, based on the time required to clear labeled platelets from circulation, has been estimated to be 8-12 days in humans. The sites for platelet removal appear to be the spleen, the liver & bone marrow. Degranulation and loss of density and platelet constituents has not been shown to decrease platelet life span indicating that the number of haemostatic interactions may not be a key component.

PLATELET ADHESION, ACTIVATION & AGGREGATION

The anti thrombotic properties of intact vascular endothelium include potent platelet inhibitors. These inhibitors include PGI_2, NO & CO which are labile molecules that are released by endothelial cells and act locally as autocoids and ADPase, an ectonucleotidase of endothelial membranes that breaks down platelet activating ADP.

Adhesion

On vascular intimal injury, the antiplatelet properties of endothelium are diminished locally, while previously cryptic, thrombogenic subendothelial substances eg. collagen become exposed to flowing blood. Circulating platelets recognize sites of vascular disruption and undergo the process of adhesion to the site of injury. Platelet adhesion is mediated by von willebrand factor which is present in the extracellular matrix of sub endothelial vessel wall. The receptor of von willebrand factor on the platelet surface is localized in membrane glyco protein (Gp) Ib, part of the platelet membrane Gp Ib / IX-V complex. Platelet adhesion is also facilitated by direct binding to subendothelial collagen by means of specific platelet membrane collagen receptors.

Activation

Adherent platelets then become activated. The platelet activation process results from the combined actions of several agonists that bind to their respective membrane receptors on adherent platelets and transmit platelet

activating intracellular signals. These platelet stimuli include humoral mediators in plasma (epinephrine, thrombin), mediator released from activated cells, (ADP serotonin), vessels wall extracellular matrix constituents that come in contact with adherent platelets (eg. collagen, von willebrand factor). Activated platelets then undergo release reaction during which they secrete prepackaged constituents of their cytoplasmic granules. The constituents released from dense granules are ADP, ATP serotonin. The constituents released from alpha granules are soluble adhesive proteins (fibrinogen, von willebrand factor, thrombospondin, fibronectin), growth factors (PDGF, TGF α, TGF β) procoagulants (platelet factor 4, Factor V). Simultaneously, activated platelets synthesize denovo and release the potent platelet activator and vasoconstrictor thromboxane A2 (TX A_2)

Aggregation

The products of the platelet release reaction, including secreted granule constituents and TXA_2 mediate aggregation. During platelet aggregation (platelet – platelet interaction), additional platelets are recruited from circulation to the site of vascular injury leading to the formation of an occlusive platelet thrombus. At lower shear levels (eg. in venous circulation), the molecular glue that mediates aggregation is fibrinogen, which can be derived either from plasma or from the alpha granule releasate of activated platelets. At higher shear level (eg. in arteries) von willebrand factor can substitute for

fibrinogen as the ligand of aggregation. Fibrinogen or von willebrand factor binds to the specific platelet membrane receptor that are located in the Gp IIb / IIIa integrin complex and mediates aggregation and finally the platelet plug is formed. The platelet plug is anchored and stabilized by the fibrin mesh that develops simultaneously as the product of the coagulation cascade.

PATHOGENESIS OF ACUTE STROKE

Ischemic stroke result from blockage of a cerebral artery by cerebral thrombosis occurring in an area of atherosclerotic plaque rupture. During the natural evolution of atherosclerotic plaques, especially those that are lipid laden, an abrupt and catastrophic chain of events may occur starting with a plaque rupture. After plaque rupture there is exposure of substances that promote platelet activation and aggregation, thrombin generation and ultimately thrombus formation. The resultant thrombus that is formed interrupts blood flow and leads to an imbalance between oxygen supply and demand and if this imbalance is severe and persistent, it leads to cerebral necrosis.

PLATELET VOLUME AND CEREBRO VASCULAR DISEASE

As the initial step in the pathogenesis of acute stroke is plaque erosion or rupture followed by platelet adhesion, activation and aggregation followed by thrombus formation, platelets with more activity will predispose to the occurrence of stroke. Mean platelet volume (MPV) correlates with platelet function and activation, whether measured as aggregation, thromboxane

synthesis, beta thromboglobulin release, procoagulant function or adhesion molecule expression (Bath et al, 1996).

Increased platelet reactivity as well as shortened bleeding time are associated with increased platelet volume (Milner and Martin, 1985; Trowbridge and Martin, 1987). Large platelets are metabolically and enzymatically more active than small platelets as assessed by in vitro aggregometry (Corash et al 1977) and they have a higher thrombotic potential (Karpatkin 1972). They also express higher levels of procoagulatory surface proteins such as P – selectin (Mathur et al, 2001) and glycoprotein III a (Pathansali et al, 2001).

Large platelets are denser and they produce more thromboxane A_2 per unit volume of platelet cytoplasm and decrease bleeding time more than control platelets. Larger platelets aggregate more rapidly upon collagen challenge, release more serotonin and other granule contents and express more receptors per unit area (Pizzuli et al, 1998).

Platelet morphology and physiology are determined during or even before fragmentation of their precursor cell, the megakaryocyte (Rabellino et al 1981). Although the mechanism is still unclear, megakaryocyte ploidy seems to correlate closely with platelet volume (Hoffman and Long 1995). Although ploidy and platelet volume are independent variables, alterations in both parameters usually occur in tandem (Trowbridge and Martin, 1987). Certain

cytokines such as Interleukin-3, thrombopoetin and in particular interleukin 6 (IL-6) seem to have a major influence on megakaryocyte ploidy leading to the production of larger and more reactive platelets (Debilli et al 1993; Brown et al 1997). Recently a frequent G/C polymorphism in the promoter region of IL-6 at nucleotide position (-174) has been shown to influence IL-6 serum levels (Fishman et al 1998). In individuals carrying the common G allele, higher IL-6 levels have been found compared to the levels in carriers of the C allele (Fishman et al 1998).

Large platelets are not necessarily young platelets (Martin et al, 1983) and there is now no convincing evidence that platelets appreciably change volume or density as they circulate (Penington, 1976).

Greisenegger et al (2004), Philip Bath et al (2004) and O' Malley et al (1994) reported an association between mean platelet volume and the occurrence of acute strokes.

Platelet volume and prognosis following acute stroke

Philip Bath et al (2004) concluded that MPV is an independent risk factor for stroke and measurement of MPV may provide useful prognostic information for clinicians managing patients with cerebro vascular disease.

Greisenegger et al (2004) observed that an elevated MPV is associated with a worse outcome for acute ischemic stroke.

AGE, GENDER AND MPV

Funiak et al (1994) observed increased MPV in patients of advanced age. In contrast Bancroft et al (2000) observed decreased MPV with advanced age. No difference between genders were detected by the latter author.

MPV AND SMOKING

Smokers were found to have an increased MPV (Tschope et al, 1989; Kario et al, 1992).

MPV AND OTHER DISEASES

An increased MPV was observed in diabetics compared to non diabetics by Sharpe et al (1993).

Although Osuna et al (1998) observed a higher MPV in patients with systemic hypertension, Bath et al (1996) observed no such effect.

Ford et al (1998) observed that patients with hyperthyroidism had increased MPV.

Bansal et al (2002) noted that MPV was increased in patients with chronic obstructive pulmonary disease and this could possibly contribute to an increased incidence of pulmonary embolism in these patients.

In chronic liver disease, MPV and platelet count have been reported to be low (Jorgensen et al, 1984).

MPV AND DRUGS

Aspirin has no effect on MPV (Pizulli et al, 1998). Recently, invitro data on the therapeutic effects of losartan, an angiotensin II receptor antagonist or Doxasosin, an alpha 1 adrenoceptor antagonist, on platelet volume have been reported (Jagroop and Mikhailidis 2001). These observation have not been confirmed in vivo (Jagroop and Mikhailidis 2000).

AIM AND OBJECTIES

1) To assess the mean platelet volume in the local population presenting with ischemic stroke and compare the same with patients presenting with hemorrhagic stroke.

2) To observe if any correlation between mean platelet volume and severity of stroke at admission and in hospital out come over 1 to 2 weeks.

MATERIALS AND METHODS

Setting	**:**	Dept of Medicine Govt. Rajaji Hospital and Madurai Medical College, Madurai
Collaborating Department :		Laboratory Services Apollo Speciality Hospital, Madurai
Design of Study	**:**	Cross Sectional Study.
Period of Study	**:**	July 2006 – June 2007
Sample Size	**:**	50 Patients and 50 controls
Ethics Committee approval :		The present project was approved by the ethics committee.

Inclusion Criteria:

Patients presenting with stroke admitted to the medical wards of Government Rajaji Hospital.

Exclusion Criteria:

1. Septicemia.
2. Hematological disorders like idiopathic thrombocytopnoea, thrombocytosis, acute leukaemia, chronic leukaemia
3. Presence of blood loss
4. Hyperthyroidism

5. Chronic liver disease
6. Chronic obstructive pulmonary disease
7. Chronic renal failure on erythropoietin therapy.
8. Known malignancies.

Controls :

Control population comprised of age and gender matched subjects without stroke and asymptomatic.

Consent :

Informed consent was obtained from all patients who participated in the study or their relatives of patients who could not sign the consent.

Materials :

A fifty patients conforming to inclusion and exclusion criteria were analysed and compared with fifty age and gender matched controls.

Definitions used for the study:

1. Stroke: was defined by an abrupt onset of a neurologic deficit that was attributable to a focal vascular cause. Thus the definition of stroke was essentially clinical and laboratory studies including brain imaging were used to support the diagnosis.

2. Systemic hypertension:

A subject was considered to have systemic hypertension if he was already diagnosed to have systemic hypertension (according to JNC VII report)

and with or without anti hypertensive medication or if there was evidence of target organ damage attributed to hypertension even if there was no past history of hypertension.

3. Diabetes Mellitus:

A subject was considered to have diabetes mellitus if he/she was already diagnosed to have diabetes mellitus or during the hospital stay was found to have a

- fasting plasma glucose of $\geq$ 126mg/dl

  Or

- 2 Hour postprandial plasma glucose $\geq$ 200mg/dl

  Or

- Symptoms of diabetes mellitus plus random blood sugar $\geq$ 200 mg /dl (according to ADA criteria)

4. Recent Acute Myocardial Infarction:

A patient was considered to have acute myocardial infarction if he / she gave a definite clinical history suggestive of acute myocardial infarction and had ECG changes suggestive of acute myocardial infarction within two weeks duration.

5. Atrial Fibrillation: defined by characteristic pattern of disogransied atrial activity without discreate p waves on the surface ECG.

6. Body mass index: = weight in kg / height in m^2

7. Smoking: A subject was considered to be a smoker if he / she gave a history of tobacco smoking within the past five years. Person who had quit smoking completely before five years were not considered as smokers.

8. Alcoholic: A subject was considered to be an alcoholic if he / she gave a history of increased alcohol intake within past five years. Persons who had quit alcohol completely before 5 years were not considered as alcoholic.

9. Physical activity should be moderate or vigorous and add up to at least 30 minutes a day

Moderate physical activities include

* Walking briskly (about 3 ½ miles per hour)
* Hiking
* Gardening /yard work
* Dancing
* Golf (Walking and carrying clubs)
* Bicycling (less than 10 miles per hour)
* Weight training (general light workout)

Vigorous physical activities include

* Running / jogging (5 miles per hour)
* Bicycling (more than 10 miles per hour)
* Swimming (freestyle laps)
* Aerobics

* Walking very fast (4 ½ miles per hour)
* Heavy yard work, such as chopping wood
* Weight lifting (vigorous effort)

10. Carotid disease was classified as whether the stenosis is symptomatic or asymptomatic and by degree of stenosis (percentage narrowing of the narrowest segment compared to a more distal internal carotid segment). Symptomatic carotid disease implies that the patient has experienced a stroke or TIA with in the vascular distribution of the artery, and asymptomatic carotid disease implies that the patient was symptom free and the stenosis is detected through screening.

11. Seizure (form the Latin sacire, "to take possession of) is a paroxysmal event due to abnormal, excessive, hypersynchronous discharges from an aggregate of central nervous system (CNS) neurons. Depending on the distribution of discharges, this abnormal CNS activity can have various manifestations, ranging from dramatic convulsive activity to experimental phenomena not readily discernible by an observer.

Methods:

Relevant socio-demographic, clinical and laboratory data were collected from the patients and controls and recorded in a proforma (Appendix I).

I. Socio demographic data comprised of :

- Age

- Gender
- History of tobacco smoking / alcoholism

II. Clinical data

- Clinical examination.

III Laboratory Data

- Blood sugar fasting and post prandial / Urea / serum Creatinine
- Lipid profile
- ECG
- Carotid doppler study
- CT Scan / MRI Brain :
- Automated complete Hemogram including platelet count and mean platelet volume

For the haematological evaluation, 2 ml of blood was drawn by venepucture after aseptic precaution and collected in EDTA coating disposable tubes from the patients within 30 minutes of admission to the hospital. The sample was transported immediately to a quality controlled centre where the sample was analysed for platelet volume. The instrument used for analysis was BECKMAN COULTER AC.T 5 DIFF 5 PART FULLY automated haematological analyzer which was repeatedly standardized for BIORAO three level quality control.

Conflict of interest:

There was no conflict of interest.

Financial support:

Nil

Limitations:

1. Technical constraints and cost factor of the investigation have led to limited number of cases.

Statistical Analysis:

Data collected were entered in Microsoft excel spread sheet and analysed utilizing the software-Epidemiological Information Package 2002 (Epi Info 2002) - developed by the centre for disease control and prevention, Atlanta for World Health Organisation and SPSS ver 15.0 was also used for the analysis. Range, Median, Mean and Standard deviation and ‘p’ values were calculated using this package. Chi squared test was used for binary and categorical data. Independent sample t-test and ANOVA were also used accordingly to test the significance between case and control groups.

OBSERVATION AND RESULTS

The total number of subjects included in the study was 100. Among the 100 subjects 50 were cases under study and 50 were controls and their profile is furnished below.

Age Distribution

The distribution of cases and controls with respect to age is given in Table – 1 given below.

Table – 1

Distribution of cases and controls with respect to age

Age Groups (years)	Case		Control	
	No	%	No	%
< 45	9	18	34	68
> 45	41	82	16	32
Range	30-88		21-67	
Median	56.50		38.50	
Mean	56.74		40.02	
S.D	12.53		10.82	
	p value = .0001 (significant) [chi-square]			

There was statistically significant difference with respect to age among them.

Gender Composition

Table 2

Distribution of cases and control with respect to gender

Gender	Case		Control	
	No	**%**	**No**	**%**
Males	41	82	30	60
Females	9	18	20	40

p value = .015 (significant) [Chi-square]

The difference in the gender composition of case and control group was statistically significant.

Weight, Height and Body mass index

Among the 50 cases, anthropometric indices was recorded in 24 cases only.

Table – 3

Distribution of cases and controls in relation to weight in kg, Height in cms and body mass index

Status		No	Range	Mean	S.D	'p' value
Weight in kgs	Case	24 (48%)	40-82	61.04	11.18	.0882 (not significant)
	Control	50	46-97	66.50	11.24	
Height in cms	Case	24 (48%)	150-176	161.17	7.1	.0263 (significant)
	Control	50	152-187	165.94	7.85	
Body mass index	Case	24 (48%)	16-31.3	23.35	3.53	.445 (not significant)
	Control	50	16.6-33.2	24.19	3.84	

There were no significant difference with respect to weight, height and body mass index among them.

Lipid Profile

Table – 4

Distribution of cases and controls in relation to Total cholesterol HDL, LDL and Triglyceride

Status		**No**	**Mean**	**S.D**	**'p' value**
Total Cholesterol	Case	50	174.20	48.36	.130 (not significant)
	Control	50	162.38	25.50	
HDL	Case	50	37.42	7.57	.075 (not significant)
	Control	50	40.60	9.96	
LDL	Case	50	112.98	38.72	.118 (not significant)
	Control	50	93.26	28.86	
Triglyceride	Case	50	126.12	59.1	0.001(significant)
	Control	50	93.26	28.86	
Total Cholesterol HDL ratio	Case	50	4.71	1.18	0.0364 (significant)
	Control	50	4.14	0.72	
	[t test]				

There were no significant differences with respect to total cholesterol, HDL, and LDL among them. There were significant difference with respect to triglyceride and total cholesterol / HDL ratio among them.

RBC count, WBC count and MCV

Table – 5

Distribution of cases and controls in relation to RBC count, Mean Corpuscular volume, and WBC counts

Status		**No**	**Mean**	**S.D**	**'p' value**
RBC counts in million/cumm	Case	50	4.56	0.68	0.072 (not significant)
	Control	50	4.79	0.54	
MCV	Case	50	83.86	8.15	.60 (not significant)
	Control	50	83.02	7.43	
WBC count in cumm	Case	50	10910	4857.83	.0001 (significant)
	Control	50	7228	1458.97	
	[t test]				

There were no statistically significant difference with respect to RBC count and MCV. There was statistically significant difference with respect to WBC count among them.

Platelet Count:

Table – 6

Distribution of cases and controls in relation to platelet count

Status		**No**	**Mean**	**S.D**	**'p' value**
Platelet count laksh in cumm	Case	50	2.52	06	.004 (significant) [t test]
	Control	50	2.88	.64	

The mean and standard deviation for platelet count of cases were 2.52 ± 0.6 lakh/cumm and those for controls were 2.88 ± 0.64 lakhs/cumm. The difference in platelet count of cases and control group was statistically significant.

Mean Platelet Volume

Table – 7

Distribution of cases and controls in relation to Mean platelet Volume (f1)

Status		**No**	**Range**	**Mean**	**S.D**	**95% CI for mean**		**'p' value**
						Lower bound	**Upper bound**	
MPV (f1)	Case	50	6.5-9.6	7.81	.79	7.591	8.031	0.145 (not significant) using ANOVA
	Control	50	6.4-8.8	7.62	0.54	7.463	7.769	

The range of MPV among cases were 6.5 – 9.6f1 and controls were 6.4 – 8.8 f1. Even though the mean MPV was higher in case than control it was not statistically significant.

Platelet count and MPV

Table – 8

Correlation between platelet count and mean platelet volume with in controls

Status		**Platelet count lakhs in cumm**	**Mean platelet volume**
Platelet count laksh in cumm	Pearson correlation	1	-.279*
	Sig (2 tailed)		.050
	N	50	50
Mean Platelet Volume (f1)	Pearson correlation	-.279*	1
	Sig (2 tailed)	.050	
	N	50	50

Control -.279* significant

The negative correlation between platelet count and MPV with in controls was statistically significant.

The negative correlation between platelet count and MPV with in cases was not statistically significant.

Table – 9

Correlation between platelet count and mean platelet volume with in cases

Correlation is significant at the 0.05 level (2 tailed)

Status		**Platelet count lakhs in cumm**	**Mean platelet volume**
Platelet count laksh in cumm	Pearson correlation	1	-.190
	Sig (2 tailed)		.187
	N	50	50
Mean Platelet Volume (f1)	Pearson correlation	-.190	1
	Sig (2 tailed)	.187	
	N	50	50

Case – Not significant

RELATIONSHIP BETWEEN MPV AND OTHER PARAMETERS

Table – 10

Relationship between Age & MPV

Age group	MPV Values				
	No	Range	Median	Mean	S.D
< 45	9 (18%)	7.0 – 9.6	7.7	8.04	.88
> 45	41 (82%)	6.5 – 9.6	7.9	7.76	.77

'p' value = .336 (not significant)

The relationship between age and MPV is not statistically significant

Table – 11

Relationship between gender & MPV

Gender	MPV Values				
	No	Range	Median	Mean	S.D
Males	41 (82%)	6.5-9.6	7.9	7.89	.81
Females	9 (18%)	6.7-8.3	7.4	7.48	.61

'p' value 0.158 (not significant)

The mean MPV for Males was 7.89 f1. the mean MPV for females was 7.48 f1. MPV was found to be independent for gender.

Table – 12

Relationship between types of stoke & MPV

Types of stroke	MPV Values		
	No	Mean	S.D
Ischemic	41 (82%)	7.72	0.67
Hemorrhagic	9 (18%)	8.26	1.12

'p' value = 0.2874 (not significant) [t test]

There was no statistically significant difference between the Ischemic stroke and Hemorrhagic stroke .

Table - 13

Relationship between Territory (ischemic) & MPV

Territory (ischemic)	MPV Values		
	No	Mean	S.D
Middle cerebral artery	27 (66%)	7.68	0.73
Posterior cerebral artery	2 (5%)	8.05	.35
Anterior cerebral artery	-	-	-
Vertebro basilar artery	7 (17%)	7.66	0.63
Multiple artery	4 (10%)	7.98	0.59

'p' value = 0.5413 (not significant) [ANOVA]

There was no statistically significant difference between the area of the ischemia and mean platelet volume.

Table - 14

Relationship between Region (Hemorrhage) and MPV

Region (haemorrhage)	**MPV Values**		
	No	**Mean**	**S.D**
Basal Gamglia	5 (55%)	8.06	1.04
Cortex	-	-	-
Thalamas	3 (34%)	8.7	1.56
Pons	-	-	-
Cerebellum	-	-	-
Others	1 (11%)	7.9	-
Multiple	-	-	-

'p' = .1188 (not significant)

There was no significant difference between the area of the hemorrhage and mean platelet volume.

Table – 15

Relationship between recurrence of stroke & MPV

Recurrence of stroke	MPV Values		
	No	Mean	S.D
YES	7 (14%)	7.53	.96
No	43 (86%)	7.86	.75

'p' = .305 (not significant)

Among 50 cases, 7 cases were recurrence of stroke and 43 cases were first episode of stroke. The mean MPV in cases with previous history of stroke was 7.53 ± 0.96fl. The mean MPV in first episode of stroke was 7.86 ± 0.75fl.

The relationship between recurrence of stroke and MPV was not statistically significant.

Table - 16

Relationship between Hypertension & MPV

Systemic Hypertension	MPV Values		
	No	Mean	S.D
YES	27 (54%)	7.76	0.71
No	23 (46%)	7.87	0.88

'p' = .624 (not significant) [t test]

There was no significant relationship between systemic hypertension and MPV.

Table - 17

Relationship between Diabetes Mellitus and MPV

Diabetes Mellitus	MPV Values		
	No	**Mean**	**S.D**
YES	19 (38%)	7.76	.72
No	31 (62%)	7.85	.83

'p' = .724 (not significant) [t test]

The relationship between diabetes and MPV was not statistically significant.

Table - 18
Correlations between lipid profile & MPV

		Mean platelet volume (f1)	**Total cholesterol**	**HDL**	**LDL**	**Triglyceride**
Mean Platelet volume (f1)	Pearson correlation	1	.076	-.015	-.002	.091
	Sig (2 tailed)		.598	.915	.992	.531
	N	50	50	50	50	50
Total Cholesterol	Pearson correlation	.076	1	.392	.906	.337
	Sig (2 tailed)	.598		.005	.000	.017
	N	50	50	50	50	50
HDL	Pearson correlation	-.015	.392	1	.253	.009
	Sig (2 tailed)	.915	.005		.076	.949
	N	50	50	50	50	50
LDL	Pearson correlation	-.002	.906	.253	1	.332
	Sig (2 tailed)	.992	.000	.076		.018
	N	50	50	50	50	50
Triglycerides	Pearson correlation	.091	.337	.009	.332	1
	Sig (2 tailed)	.531	.017	.949	.018	
	N	50	50	50	50	50

There was no correlation between lipid profile and mean platelet volume.

Table - 19

Relationship between recent myocardial infarction & MPV

Recent myocardial infarction	MPV Values		
	No	Mean	S.D
YES	4 (8%)	7.8	0.52
No	46 (92%)	7.82	0.81

'p' = .971 (not significant) [t test]

There was not significant difference between recent myocardial infarction and MPV

Table - 20

Relationship between Valvular Heart Disease & MPV

Valvular Heart disease	MPV Values		
	No	Mean	S.D
YES	1 (2%)	8.2	-
No	49 (98%)	7.81	.79

'p' = .625 (not significant)

The relationship between valvular heart disease and MPV was not statistically significant.

Table - 21

Relationship between smoking & MPV

Smoking	MPV Values		
	No	Mean	S.D
YES	15 (30%)	8.14	.86
No	35 (70%)	7.67	.72

'p' = .054 (Significant) [t test]

Among the 50 cases, 15 cases were smokers and 35 cases were non smokers. The mean MPV among smokers was 8.14 f1. The mean MPV among non smokers was 7.67 f1. A significant relationship between smoking and MPV was noted.

Table - 22

Relationship between Alcohol & MPV

Alcohol abuse	MPV Values		
	No	Mean	S.D
YES	19 (38%)	8.12	.69
No	31 (62%)	7.63	.79

'p' = .032 (Significant) [t test]

Among 50 cases 19 cases were alcoholic and 31 cases were non-alcoholic. The mean MPV among alcoholic was 8.12 f1. The mean MPV among non alcoholic was 7.63 f1. There was significant relationship between alcohol and MPV.

Table - 23

Relationship between physical activity & MPV

Physical activity	**MPV Values**		
	No	Mean	S.D
YES	48 (96%)	7.83	0.80
No	2 (4%)	7.50	.28

'p' = .569 (not significant) [t test]

There was no significant relationship between physical activity and MPV

Table - 24

Relationship between carotid stenosis & MPV

Carotid Stenosis	**MPV Values**		
	No	Mean	S.D
> 70% occlusion	2 (4%)	8.9	0.42
< 70% occlusion	25 (50%)	7.59	0.64

'p' = .05 significant (ANOVA)

Among 41 cases of ischemic stroke, in 27 cases Carotid doppler study was done. Two cases had more than 70% carotid occlusion and 25 cases had less than 70% carotid occlusion.

There was a statistical significance noted between carotid stenosis and MPV

Table - 25

Relationship between Hemorrhagic transformation of Infarction & MPV

Age transformation of Infection	**MPV Values**		
	No	Mean	S.D
YES	4 (8%)	7.03	0.41
No	39 (78%)	7.74	.68

'p' = .0009 (significant) (ANNOVA)

Among 50 cases, 4 cases had hemorrhagic transformation of infarction, 39 cases had no hemorrhagic transformation. The mean MPV for hemorrhage transformation of infarction was 7.03 f1. The mean MPV for patients with pure infarction with no haemorrhage transformation was 7.74 f1. There was a statistically significant relationship between hemorrhagic transformation of infarction and MPV.

Table - 26

Relationship between Aspirin & MPV

Aspirin medication before admission	**MPV Values**		
	No	Mean	S.D
YES	13 (26%)	7.58	.82
No	37 (74%)	7.90	.77

'p' = .3857 (not significant) [t test]

No significant relationship between aspirin medication before admission and MPV was noted

Table - 27

Relationship between clopidogrel & MPV

Before admission clopidogrel intake	**MPV Values**		
	No	Mean	S.D
YES	9 (18%)	7.79	.87
No	41 (82%)	7.82	.78

'p' = .0232 (Not significant) [t test]

No significant relationship between clopidogrel intake before admission and MPV

Table - 28

Relationship between LMW Heparin & MPV

Before admission LMW Heparin	MPV Values		
	No	Mean	S.D
YES	3 (6%)	8.2	.95
No	47 (94%)	7.79	0.78

'p' = .6047 (not significant) [t test]

Table - 29

Relationship between Regular Heparin & MPV

Before admission Regular Heparin	MPV Values		
	No	Mean	S.D
YES	2 (4%)	8.75	.64
No	48 (96%)	7.78	.77

'p' = .2035 (not significant) [t test]

Table - 30

Relationship between Warfarin & MPV

Before admission Warfarin	MPV Values		
	No	Mean	S.D
YES	1 (2%)	8.3	-
No	49 (98%)	7.86	.79

No significant relationship between LMW heparin, regular heparin and warfarin with mean platelet volume.

Table – 31

Relationship between Inj. Mannitol & MPV

Before admission injection mannitol	MPV Values		
	No	Mean	S.D
YES	6 (12%)	8.4	.69
No	44 (88%)	7.76	.79

'p' = .2788 (not significant) [t test]

Table - 32

Relationship between Glycerol & MPV

Before admission Glycerol	MPV Values		
	No	Mean	S.D
YES	3 (6%)	8.53	.6
No	47 (94%)	7.77	.80

'p' = .1675 (not significant) [t test]

Table - 33

Relationship between Statin & MPV

Before admission Statin	**MPV Values**		
	No	**Mean**	**S.D**
YES	8 (16%)	7.51	.80
No	42 (84%)	7.87	.78

'p' = .4003 (not significant) [t test]

No significant relationship between injection mannitol, glycerol and statin with mean platelet volume.

Table - 34

Relationship between Ramipril & MPV

Before admission Ramipril	MPV Values		
	No	Mean	S.D
YES	2 (4%)	6.7	.28
No	48 (96%)	7.86	.77

'p' = .0048 (Significant) [t test]

Among 50 cases, two cases were on Ramipril before admission and 48 cases were no Ramipril intake before admission

Table - 35

Control Vs Before admission Ramipril intake relation to mean platelet volume

Status	MPV Values		
	No	Mean	S.D
Control	50	7.62	0.54
Before admission Ramipril	2	6.7	0.28

p value = .0130 (significant) [t test]

Table – 36

Control Vs Before admission not taking Ramipril

Status	MPV Values		
	No	Mean	S.D
Control	50	7.62	0.54
Before admission Not taking Ramipril	48	7.86	0.77

p value = .2083 (not significant)

There was significant relationship between Ramipril use before admission and MPV

Table – 37

Association between severity of stroke (modified Rankin scale) during admission and MPV

Severity of stroke mRS scale	MPV Values					
	No	Range	Median	Mean	95% CI for mean	S.D
0-2 (upto slight disability)	5 (10%)	6.8-8.1	7.300	7.44	6.657-8.223	.63
3-5 (moderate to severe disability)	45 (90%)	6.5-9.6	7.900	7.860	7.616 – 8.095	.80

p value = .266 (not significant) [t test]

During admission patient with moderate to severe disability of the stroke had higher mean MPV than slight severity of stroke, but it was not statistically significant.

Table – 38

Association between stroke severity according to Glasgow out come score during discharge and MPV

Severity of stroke as per Glasgow outcome score during discharge	MPV Values					
	No	Range	Median	Mean	95% CI for mean	S.D
5 (Good recovery)	13 (26%)	6.8 – 9.6	7.4	7.71	7.19-8.22	.85
4 (moderate disability)	19 (38%)	6.5 – 9.2	7.9	7.77	7.38-8.16	.81
3 (severe disability	15 (30%)	7.0 – 9.6	7.9	7.94	7.57-8.31	.67
2 (Persistent vegetative state	3 (6%)	6.5 – 8.8	8.4	7.9	4.85 – 10.95	1.23
1 (Death)	0	-	-	-	-	-

During discharge the patient with severe disability of stroke had higher mean MPV than good recovery of stroke, but it was not statistically significant.

DISCUSSION

Stroke is a world wide social and health problem. It makes an important contribution to morbidity, mortality and disability in developed as well as developing countries like India. Endogenous and exogenous risk factors like systemic hypertension cardiac abnormality, diabetes mellitus, dyslipidema, obesity and smoking significantly increase the risk for stroke. However they only explain part of the problem and in some of the cases there may be other relevant risk factors which need to be identified and addressed.

Bath et al (2004) found that mean platelet volume (MPV) is an independent risk factor for stroke. Similar observations were made by O' Malley et al (1995) and Greisenegger et al (2004). Large platelets are more reactive, produce more thrombotic factors (Martin et al, 1982) and aggregate more easily (Haver et al, 1981). However most studies are from the west with healthy western people serving as controls. An attempt was made in present study to find out if any association existed between the platelet size and occurrence of stroke among the local population. Currently, no data are available regarding this aspect among Indian population.

In this study, the age of the cases ranged from 30-88 years. The mean was 56.74 ± 12.53 years. Maximum number of cases i.e. 41 cases fell in the age above 45 years (82%). This is in parallel with the observation made by Henry et

al (1998) and Park K (2005). This may be probably due to ongoing atherosclerosis as age advances.

Available literature on association between age and MPV is contradictory with evidences showing both an increase in MPV with age as observed by Funiak et al and also decrease in MPV with age shown by Bancroft et al. In the present study no statistically significant relation was noted between age and MPV and similar to the observation also made by Von Behren et al. While advancing age is associated with increased incidence of stroke and increased mean platelet volume also increased the incidence of stroke, the lack of direct association between increasing age and MPV is interesting yet puzzling. Presumably the smaller sample size in our data was responsible for this observation.

Among 50 cases, there were 41 men (82%) and 9 (18%) women. Park K (2005) noted that incidence rates are higher in males than females at all ages. This gender difference is due to different vascular risk factor profile among men and women namely alcoholism and smoking for men, hypertension and cardio embolism for women. Gender specific incidence rate converge after menopause suggesting a major role for estrogen in delaying progression of atherosclerosis. Much of this effect results from beneficial action of estrogen on lipid fraction. Estrogen reduces LDL – C by 10-15% while increasing HDL-C.

In the present study MPV was independent of gender. Bancroft et al (2000) noted that MPV was independent of gender. Our study confirms the observation made by the above author.

In our study, among 50 cases, 41 cases (82%) had ischemic stroke and 9 (18%) had hemorrhagic stroke. Henry JM et al (1998) observed that 70% of stroke cases were ischemic in nature and 27% were hemorrhagic. Furlan et al (1979) had also noted that the incidence of primary hemorrhagic stroke was low. Our study is in parallel with these observations. In our study incidence of hemorrhagic stroke was low. This may be due to early detection and treatment for systemic hypertension which is the most common cause of intracerebral hemorrhage.

In our study though the mean of MPV was higher in the hemorrhagic strokes than ischemic strokes. This difference was not statistically significant. Bath et al (2004) found values of MPV for ischemic stroke were higher and there was no evidence of association of MPV with either intracerebral hemorrhage (or) stroke of unknown etiology. Eldor A et al (1982) had noted that increase in MPV, reduced the occurrence of hemorrhage stroke contradictory to our findings

Among the 41 cases of ischemic stroke.

27 cases (66%) had middle cerebral artery infarct

2 cases (5%) had post cerebral artery infarct

7 cases (17%) had vertebro basilar territory infarct

4 cases (10%) had multiple vessel infarction and

1 case (2%) had cerebral venous thrombosis

No patients had anterior cerebral artery infarct. Middle cerebral artery is a direct branch of internal carotid artery. This artery is most vulnerable for thrombo embolic infarction rather than other branches of internal carotid artery Adam et al (1961). There was no statistically significant difference between the territory ischemic involvement and MP. It is thus unlikely that platelet consumption at any particular thrombus site would affect the peripheral venous estimation of platelet variable.

In our study, among 9 cases of hemorrhagic stroke, the lesions were localised in the following areas of the brain.

5 cases (55%) had basal ganglionic involvement

3 cases (34%) had thalamic involvement

1 cases (11%) present with primary intra ventricular hemorrhage

In general basal ganglion is the commonest area involved in hemorrhagic stroke Wade et al (2005). There was no statistically significant relationship between the region of hemorrhage and MPV.

In our study, 17 cases had right hemispherical lesion, 28 cases had left hemispheric lesion and 5 cases had bilateral hemispheric involvement of both

the hemisphere. Common carotid artery occlusion by atheromatous plaque at its origin was seen more often on the left side (Ropper et al).

In the present study among 50 cases, 7 cases (14%) had presented with recurrence of stroke. There was no statistically significant relationship between recurrence of stroke and MPV. O'Malley et al observed that there was no significant difference in MPV in patients with previous history of stroke compared to patients with no previous stroke. Our finding runs in parallel with this observation. Thus it may be inferred that increase in MPV could influence the occurrence of stroke, but not whether there could be recurrence. Thus targeting therapeutic strategy in future to reduce the MPV may not be useful in the secondary prevention of stroke though this could be of value in the primary prevention.

Duration between onset of stroke to seek medical help, ranged between 10 minutes to 2880 minutes. Mean ± SD was 175.80 ± 563.27 minutes. Duration between onset of stroke to reach tertiary care hospital ranged between 30-4320 minutes. Mean ± SD was 1217.50 ± 1243.66 minutes.

In our study, the reasons for delay were as follows

84% due to local hospital treatment

12% due to transport delay

4% due to financial problems

Bath et al (2004) study showed that the time of MPV measurement, the time of occurrence of stroke or delay between blood collection and measurement of MPV did not alter the MPV significantly.

Distance traveled to reach the tertiary hospital ranged between 2-200km. Time interval from onset of stroke to take CT/MRI scan of brain ranged from 40-2940 minutes. Door to aspirin / clopidogrel timed ranged from was 110-960 minutes. Among the stroke patients, 27 cases (54%) had systemic hypertension. The prevalence of systemic hypertension in stroke was 80.8% in the Framingham study 1950. In general with systemic hypertension there was 50% chance of increase risk for stroke. Systemic hypertension was responsible worsening of atherosclerosis.

However in the present study, no statistical relationship was observed between systemic hypertension and MPV. Bath et al (1996) had earlier made observation similar to our study. Osuna et al (1998) and Cardee et al (1981) observed a higher MPV in those with systemic hypertension presenting with acute myocardial infarction. This may be due to change is megakarocyte processing and thrombopoietin in response to change in vascular function in hypertension.

Despite atherosclerosis being common for both acute myocardial infarction and stroke, whether regional difference in the target organ damaged

contributed to such a discrepancy is not known as our study was done on stroke while Osuna et al reported on myocardial infarction.

Nineteen patients (38%) in the present study had diabetes mellitus. However the MPV of patients with diabetes mellitus did not vary from those without diabetes mellitus. Sharke et al (1993) noted that MPV was significantly increased in diabetic subjects compared with nondiabetic. They stated that since the platelet size is a determinant of platelet function, with larger platelets being more reactive per unit volume, the platelets might play a part in the micro and macro vascular complications of diabetes mellitus.

Osuna et al (1998) also observed a higher MPV with diabetes mellitus. This may be due to diabetes related stem cell dysfunction of megakaryocytic series and its progenitor cells resulting in increased MPV and reactivity. The fact that in our study no relationship was observed may be due to the small sample size. Whether the degree of diabetic control could have influenced this effect was not specifically looked of in this study.

Kario et al (1992) had reported that hypercholesterolemia was associated with increase in MPV. In our study no correlation existed between lipid profile and MPV. Thus MPV may be considered as on independent risk factor for stroke. This is also strengthened by our observation that use of statin did not influence MPV. A positive correlation between total cholesterol with HDL, LDL and triglyceride was found in the present study. There was no correlation

between HDL, with LDL and triglyceride. There was positive correlation between LDL and triglyceride. Greisenegger et al (2004) found that there was no significant correlation between MPV and serum cholesterol and triglyceride levels.

In the present study 4 cases (8%) had recent myocardial infarction. All 4 cases involved the anterior myocardial wall. In general population 2-6% of stroke cases were due to emboli from left ventricle mural thrombus which was not detected by echo in 40% of cases of anterior myocardial infarction.

Martin et al (1983) and Cameron et al (1983) found an association between increased mean platelet volume and increased occurrence of myocardial infarction. However studies conducted by Halbmayer et al (1995) and Bath et al (2004) showed that coronary event rates were not associated with MPV. Our finding runs in parallel with that of Halbmayer et al (1995) and Bath et al (2004). The absence of an association of MPV with coronary events could reflect a true lack of association in this study population. A more likely explanation is that the small number of coronary events provided only limited statistical power to detect the true association of MPV with coronary disease.

Among 50 cases, fifteen (30%) were smokers. This shows an increased prevalence of smoking among patients with stroke and this was statistically significant. Wolf et al (1988) observed that cigarette smoking was a risk factor for stroke. Framingham study et al (1988) found a 50% increased risk of stroke

in smokers than non smokers. In smokers hemorrhagic stroke was two times more common than ischemic stroke. Smoking causes temporary increase in blood pressure which acting in concert with metastatic emphysema effect was responsible for subarachnoid hemorrhage from cerebral aneurysm.

MPV was higher among smokers compared to non smokers and this relationship was statistically significant. Tschope et al (1989) and Kario et al (1982) in separate studies found smokers to have an increased MPV. However Kishk et al (1985) observed no relation between smoking and MPV. Our finding runs in parallel with that of Tschope et al (1989) and Kario et al (1982). Smoking, due to direct stimulation of thrombopoietin production results in increased absolute count of reticulocyted platelet with higher MPV and containing higher concentration of p selection in per unit volume of platelet.

In the present study, 19 cases (38%) consumed alcohol, Gerelick et al (1989) found that alcohol was an independent risk factor for stroke. In the present study MPV was higher among who consumed alcohol and this effect was statistically significant. One explanation may be the coexistence of smoking with alcoholism, as MPV is known to be high in smoker. Donahue et al (1986) reported that alcohol consumption was related to hemorrhagic stroke than ischemic stroke and a ‘U’ shaped relationship between level of alcohol consumption and ischemic stroke. Minimal alcohol consumption or total abstinence and heavy alcoholic consumption were associated with increased

risk for stroke. Modest alcohol consumption reduced risk for stroke. Risk for hemorrhage stroke in patients who consumed alcohol was due to sudden increase in blood pressure on a background of sustained decrease in cholesterol level which weakened the vessel walls. Associated smoking also worsened this effect.

In our study 48 patients (98%) were physically active prior to onset of stroke. There was no statistically significant difference between physical activity and MPV, which may be due to the small sample size. Physical activity exerts a beneficial influence on risk factors for atherosclerosis.

In our study, 2 cases (4%) had symptomatic carotid stenosis with more than 70% occlusion. There was statistically significant difference between carotid stenosis and MPV. In the general population, 5% of carotid atherosclerosis cause ischemic stroke (Wade S et al).

Among 40 cases with ischemic stroke, 4 (8%) developed hemorrhagic transformation of the infarct. Among these 4 cases, one case had cerebral venous thrombosis and other 3 patients had been already on aspirin medication for previous stroke. There was significant statistical relation between hemorrhagic transformation of infarction and MPV. This observation is clinically relevant as this may guide the clinician to be proactive in following patients with acute ischemic stroke to look for hemorrhagic transformation in those with increased MPV.

Among 50 cases, 13 had taken aspirin before admission. There was no significant relationship between those who had aspirin intake before admission and MPV.

Pizulli et al (1988) stated that aspirin has no effect on platelet volume. Contrary to their observation Bath et al (2004) found marked differences in of MPV with use of antiplatelet therapy. The difference in MPV between participants who were on or off antiplatelets were small in the present study. Greisenegger et al (2004) also found that patients on prior aspirin medication had significantly higher MPV values, possibly because of a higher vascular premorbidity. Aspirin increases the MPV by inhibiting cyclooxygenase pathway which influences the metabolic and signaling aspect of ‘p’ selectin in the megakarocyte.

Among 50 cases 9 had taken clopidogrel before admission. There was no statistically significant relationship between clopidogrel intake and MPV. In vitro studies have revealed that clopidogrel inhibits the ADP induced increase in MPV Greiseneger et al 2004.

Among 50 cases, 3 were on low molecular weight heparin, 2 were on regular heparin and one was on warfarin before admission. There were no significant relationships between LMW heparin, regular heparin, and warfarin with MPV. Thus while heparin is known to be associated with

thrombocytopenia no effect was noted on the volume of the individual megakaryocyte.

Among 50 cases, 5 were on injection mannitol and 3 had received glycerol before admission. No significant relation was found between the use of injection mannitol and glycerol and MPV.

Among 50 cases 8 were on statin before admission. Association between MPV and statin usage was not statistically significant.

Among 50 cases 2 were found to have been on ramipril before admission, and this had a statistically significant relationship with MPV. Bath et al (2004) noted that the antiplatelet activity of perindopril and other ACE inhibitors appear to have little effect on MPV.

In the present study use of ramipril was noted to decrease MPV significantly an observation made in both the stroke population and healthy controls. Thus this drug may have an independent effect in influencing stroke severity.

In the present study, distribution of cases and controls in relation to RBC count and mean corpuscular volume were not statistically significant.

However the distribution of cases and controls in relation to WBC count was statistically significant. Gresienegger et al (2004) stated that no significant correlation existed between MPV on admission and leukocyte count. Bath et al (2004) observed that severe stroke was associated with increased WBC counts.

Findings of the present study run in parallel with the observation made by the latter author.

Gilea et al (1984) observed that not all acute illness are associated with raised MPV. This may be due to some of the cytokines like interleukin 3, Granulocyte megakaryocyte colony stimulating factor may influence both megakaryocyte progenitor and myeloid progenitor at bone marrow level.

The mean platelet count of cases in this study was 2.52± .06 lakhs/mm3 and that of control was 2.82± .64 lakhs /mm3 a difference that was statistically significant. O'Malley et al (1994) stated that platelet count was reduced in stroke patients compared with control groups. MPV was higher in acute stroke compared with control subject.

Greisenegger et al (2004) observed a slight but significant negative correlation between MPV and mean platelet count. There was negative correlation between platelet count and MPV among controls and this was statistically significant. There was a similar negative correlation between platelet count and MPV within cases, though this observation did not reach the level of statistical significance.

O' Malley et al (1994) observed that there was a significant negative correlation between platelet count and MPV in stroke patients. It was statistically significant. There was no such correlation between platelet count

and MPV in control subjects. Although MPV among cases was higher compared to control it was not statistically significant.

O'Malley et al (1995) conducted a similar study of MPV estimation in stroke patients. They estimated MPV in stroke patients within 48 hours of admission and also at 6 months follow up and compared it with controls. They found that MPV was significantly raised in stroke patients compared to controls. They suggested that the changes in MPV might have preceded the vascular event and is unlikely to be due to platelet consumption at the infarct site. They said that since the average life span of the platelets is about 8 days, the elevated MPV seen within the first 48 hours after stroke represented platelets released before infarction. Furthermore it was unlikely that platelet consumption due to the localized thrombosis would affect peripheral venous estimation of platelet variables. They further stated that since there was no difference in MPV between large cortical strokes and small lacunar infarcts, it was unlikely that platelet consumption at the thrombus site would affect the peripheral venous estimation of platelet variables. They also added that the fact that the observed increase in MPV had remained unchanged in post stroke survivors was further evidence that changes in MPV were likely to have preceded the acute event.

Bath et al (2004) conducted a similar study of MPV estimation in stroke patients. MPV was positively associated with occurrence stroke and

measurement of MPV may add useful prognostic information for clinician managing patients with history of cerebrovascular disease. This study concluded that there was no clear association of MPV with risk of major coronary events. However it is to be acknowledged that the small number of coronary events provided only limited statistical power to detect the true association of MPV with coronary events.

During admission, patients with moderate to severe disability due to stroke (modified Rankin Scale 3-5) had higher MPV than patients with lesser disability due to stroke (mRS 0-2) however this was not statistically significant. During discharge patient with moderate to severe disability due to stroke had higher MPV then those who made good recovery, through this differences was not statistically significant.

Our observation are in contrast to this by Greisenegger et al (2004) who noted that elevated MPV is associated with worst outcomes for acute ischemic cerebrovascular events independent of other clinical parameters. In severe stroke, increased MPV reflects higher platelet reactivity before stroke has occurred. O Framo et al (1990) and O' Malley et al (1999) stated that no relationship existed between MPV and stroke outcome. Possible reasons for these divergent results could be the small number of patient and the use of different outcome measures in these studies.

Thus it may be concluded that while the occurrence of stroke may be influenced by MPV, severity of stroke at admission or discharge is independent of the degree of elevation of MPV. Thus MPV may not be useful as prognostic marker following stroke.

Strengths, Limitations and future recommendation

This study is the first to address to role of MPV in stroke population in India . Ethnic differences in stroke being well established, this may provoke future research to understand the significant is that MPV in the pathogenesis of stroke in a large context. Small sample size was the major limitation in this study however.

Areas of further work

1. MPV studies in other thrombotic episodes
2. Follow up study on MPV after the onset of clinical events.
3. Platelet volume studies among patients on losartan and doxasosin.
4. In vitro studies on factors contributing for thrombomegaly in order to introduce interventional measures
5. Studies to find out the physiological measurements which regulate MPV within the megakaryocyte.

SUMMARY

The study ‘mean platelet volume in cerebro vascular disease’ was undertaken to assess the relationship between mean platelet volume (MPV) and various aspects of stroke. Fifty patients who presented with stroke to a tertiary care hospital were studied. The demographic, clinical and laboratories data of these patients were recorded. The relationship between mean platelet volume and the type of stroke, age, gender, conventional risk factor and treatment aspects were analysed. MPV in these patients were compared to controls who were age and gender matched.

There was no significant relationship between age, gender, type of stroke, territory of arterial involvement in ischemic stroke, region affected in hemorrhage stroke, recurrence of stroke, systemic hypertension, diabetes mellitus, recent myocardial infarction, valvular heart disease, physical activity with MPV.

There was significant negative correlation between platelet count and MPV in control groups. In cases there was negative correlation between platelet count and mean platelet volume but it was not statistically significant.

MPV was higher with smoking, alcohol use and carotid stenosis more than 70%. MPV was lower than normal in patients with hemorrhagic transformation of infarction and with intake of ramipril in the cases. No

significant relationship between intake of drugs like aspirin, clopidogrel, LMW heparin, regular heparin, warfarin, statin, injection mannitol and oral glycerol with MPV.

The mean platelet count in cases 2.52± 0.06 lakh/mm^3 and the mean platelet count in control 2.88±0.64lakh/mm^3 (p=.004 statistically significant). The MPV of the patients ranged from 6.5-9.6 femtolitres and controls ranged from 6.4-8.8 femtolitres. The Mean and SD of MPV of the patient was 7.81±..7 femtolitres and that of control was 7.62±0.54 femtolitres. This was not statistically significant (p=.315). The mean value of mean platelet volume was higher among the patients with haemorrhagic stroke compared to those with ischemic stroke, though the difference was not significant.

MPV was higher in patients with moderate to severe disability due to smoke than those with lesser disability due to during admission as well as discharge following acute care. This was not statistically significant.

Pathophyiology of increased MPV may need to be further elucidated and its clinical bearing has to the studied involving larger studies.

Further research is required into the role of platelet volume in stroke pathology and outcome and also importantly in influencing the individual risk factors of stroke. Whether MPV becomes a routinely requested test remains to be seen.

CONCLUSION

- MPV was elevated in the patients with stroke when compared to control in a non significant manner.

- The mean value of mean platelet volume was higher among the patients with haemorrhagic stroke compared to those with ischemic stroke, though the difference was not significant.

- MPV was higher among the patients with moderate to severe disability of stroke than patients with slight disability of stroke in a non significant manner.

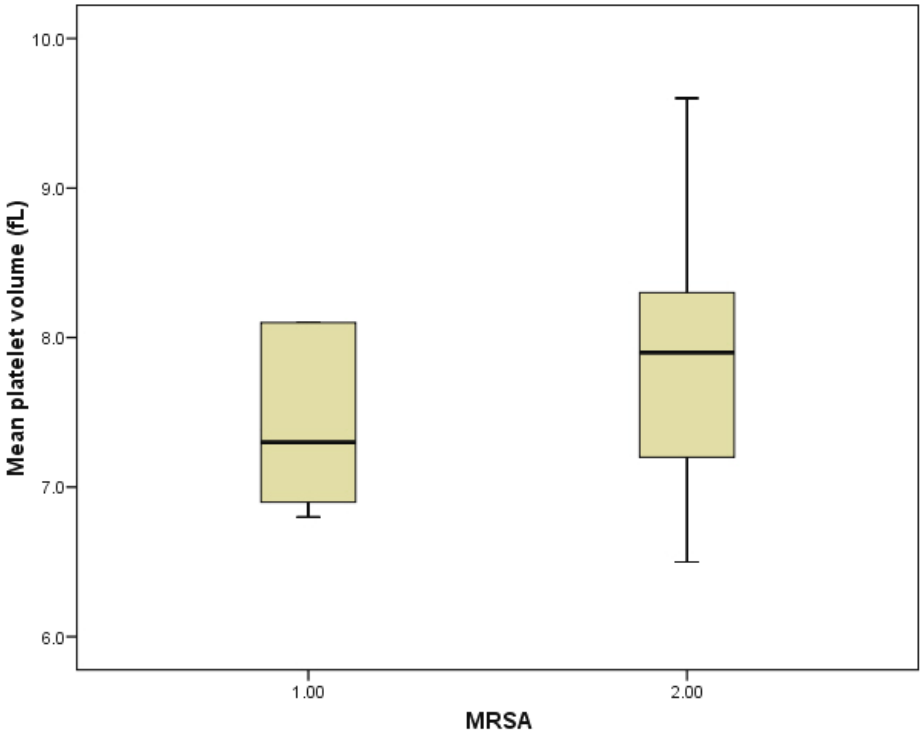
- There was significant negative correlation between platelet counts and MPV in controls. In cases also there was negative correlation between platelet counts and MPV though it was not significant.

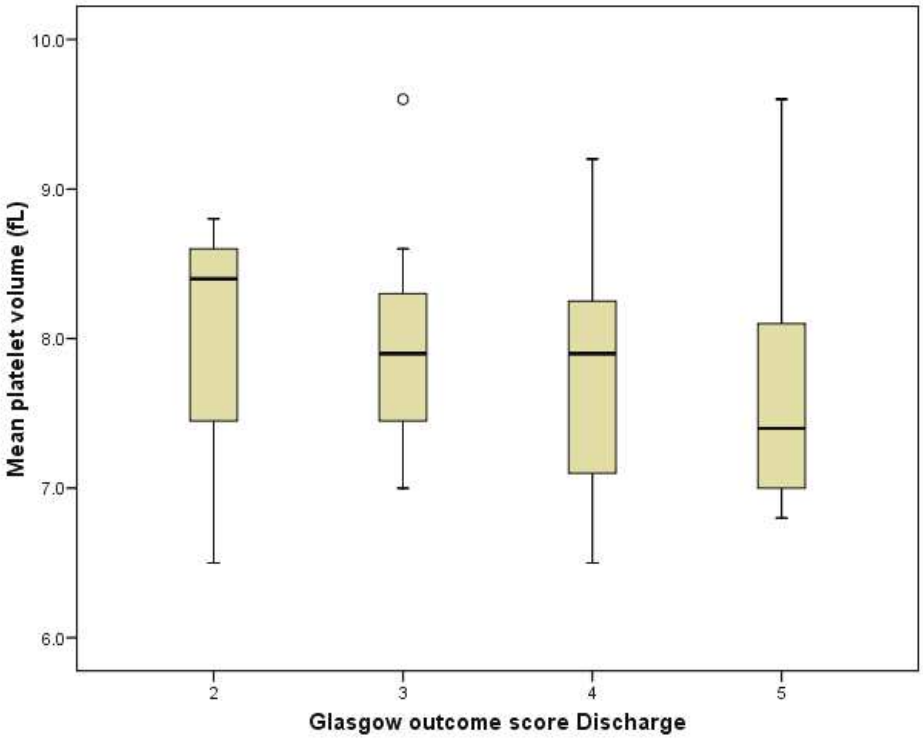
- There was no correlation between lipid profile and MPV in cases.

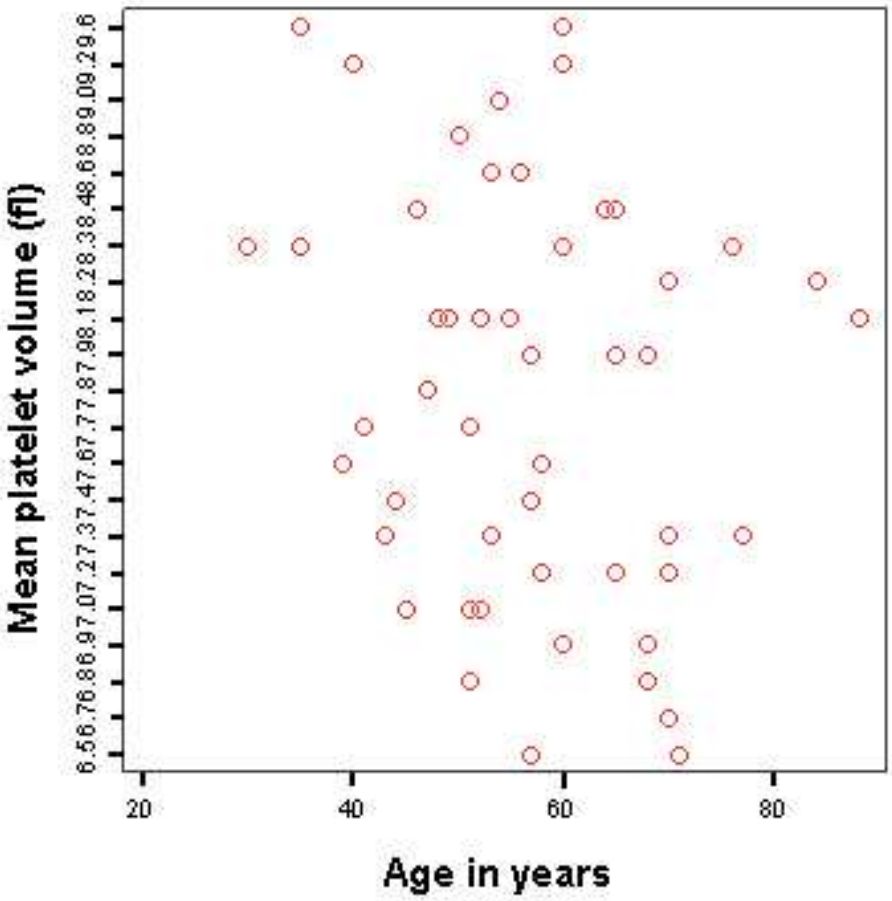
- MPV was higher among smokers, alcoholics and patients with carotid stenosis more than 70% occlusion.

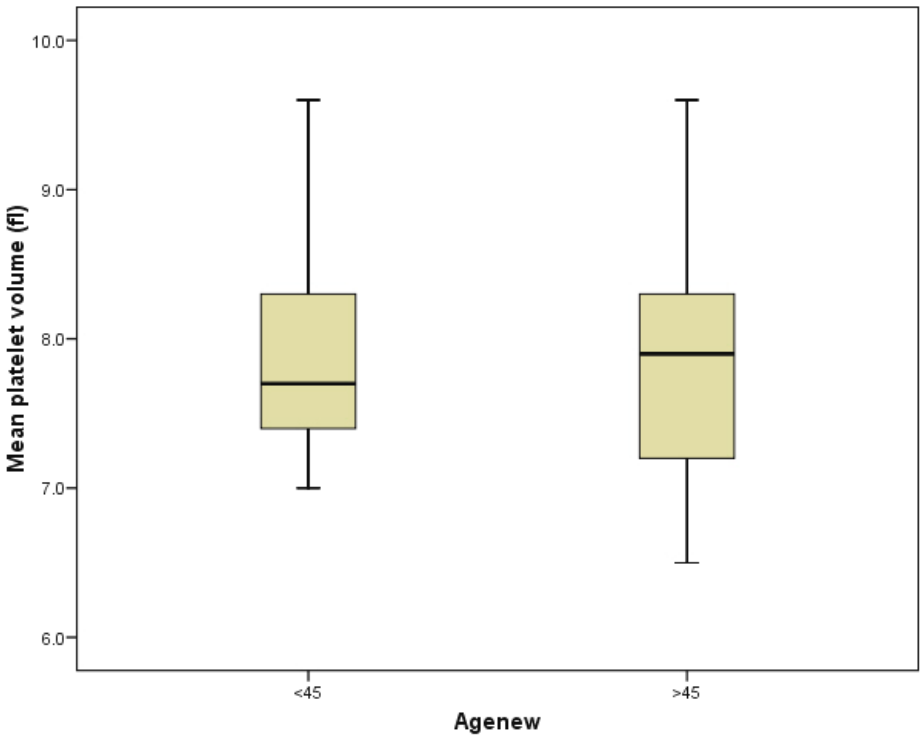
- MPV was lower among the patients with hemorrhagic transformation of infarction and Ramipril intake.

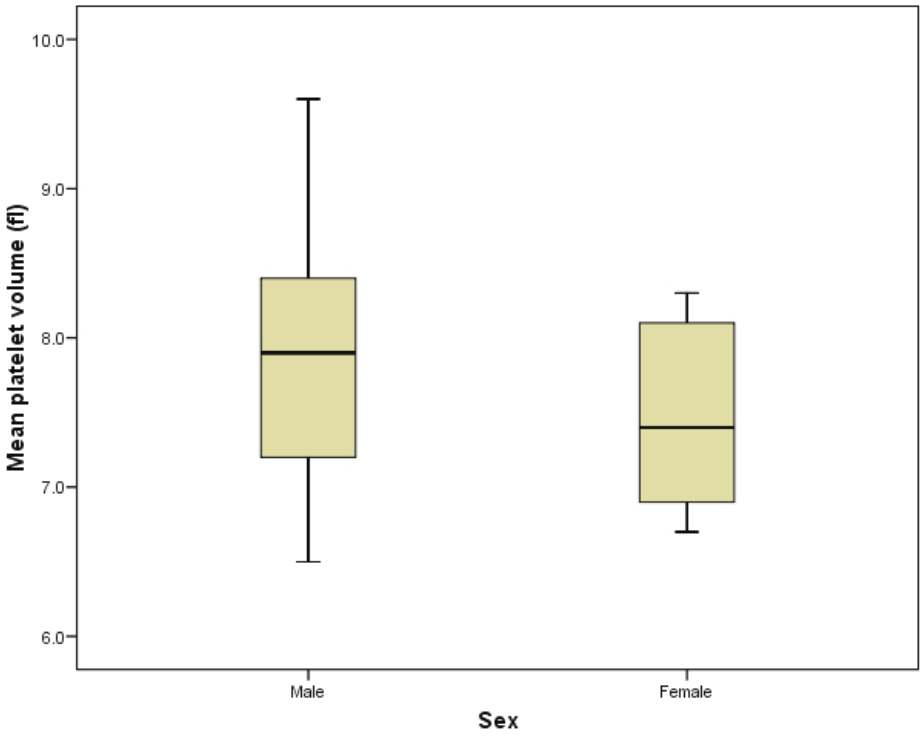
- MPV in patients with stroke was found to be independent of age, gender, type of stroke, territory of ischemia, region of hemorrhage, recurrence of stroke, hypertension, diabetes mellitus, recent myocardial (ischemic) infarction, valvular heart disease, physical activity, drugs like aspirin clopidogrel, LMW heparin, regular heparin, warfarin, injection mannitol, oral glycerol and statin.

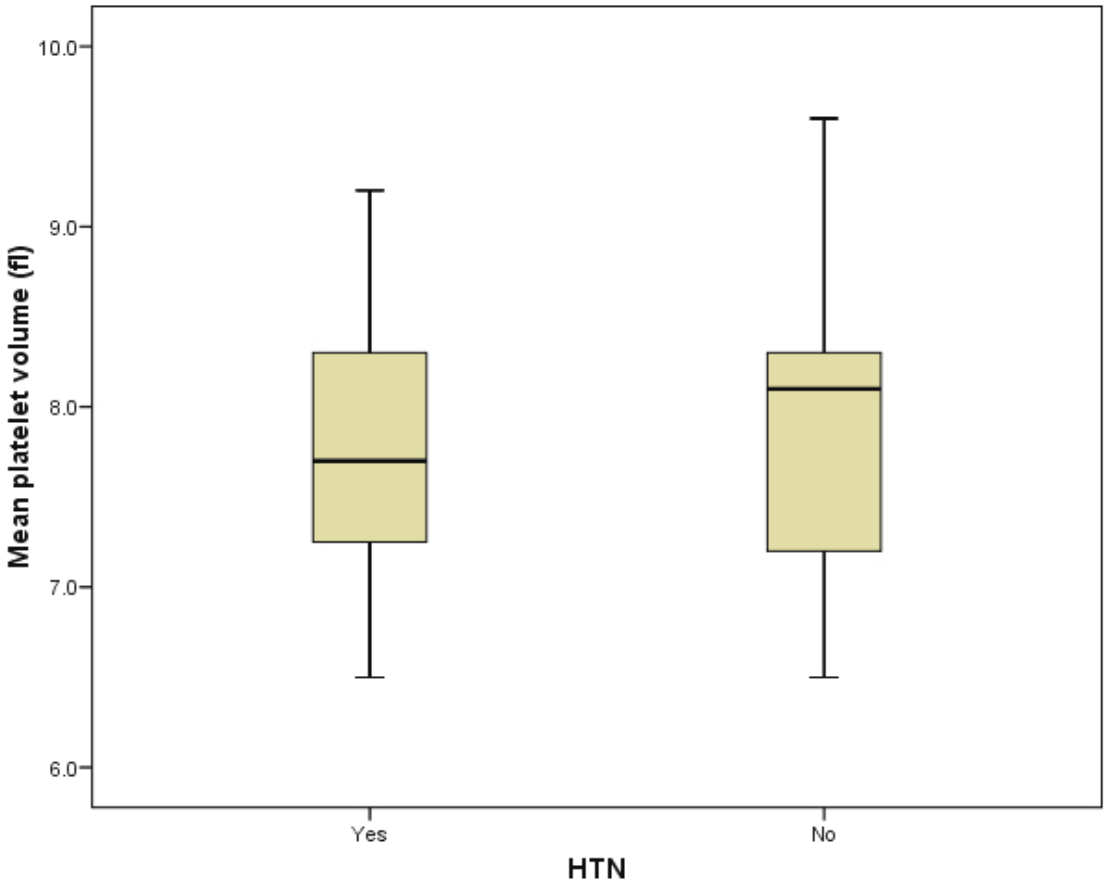

Mean platelet volume (fL)
10.0
9.0
8.0
7.0
6.0
1.00
2.00
MRSA


Mean platelet volume (fL)
10.0
9.0
8.0
7.0
6.0
2
3
4
5
Glasgow outcome score Discharge


Mean platelet volume (fl)
6.5
6.7
6.8
6.9
7.0
7.2
7.3
7.4
7.6
7.7
7.8
7.9
8.1
8.2
8.3
8.4
8.6
8.8
8.9
9.0
9.2
9.6
20
40
60
80
Age in years


10.0
9.0
8.0
7.0
6.0
Mean platelet volume (fl)
<45
>45
Agenew


10.0
9.0
8.0
7.0
6.0
Mean platelet volume (fl)
Male
Female
Sex


10.0
9.0
8.0
7.0
6.0
Mean platelet volume (fl)
Yes
No
HTN

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MEAN PLATELET VOLUME IN STROKE – CASE STUDY

Sl. No.

Hospital No.

Name

Age

Gender

M	1	

F	2	

Type of stroke

Ischemic	1	

Hemorrhagic	2	

Territory (Ischemic)

MCA	1	

PCA	2	

ACA	3	

VBI	4	

Multiple	5	

Not applicable	9	

Region (Hemorrhage)

Basal Ganglia	1	

Cortex	2	

Thalamus	3	

Pons	4	

Cerebellum	5	

Others	6	

Multiple	7	

Not applicable	9	

Hemisphere

R	1	

L	2	

Both	3	

Recurrence of stroke

Y	1	

N	2	

Duration between onset of stroke to seeking medical help first (minute)

Duration to reach Territory Hospitals – Madurai (minute)

Reason for delay

Local	1	Transport delay	2	Financial problem	3	Other	4

Distance from Territory hospital

Door to CT/MRI (minutes)

Door to Aspirin / Clopidrogel (minutes)

Hypertension	Y	1		N	2
HT (in year)					
Diabetes	Y	1		N	2
DM (in year)					
Dyslipidemia	Y	1		N	2
Recent myocardial infarction	Y	1		N	2
Valvular heart disease	Y	1		N	2
Atrial fibriliation	Y	1		N	2

Nutritional status (BMI)

Wt	<18.5	1		18.5 -24.9	2		
Ht	25-29.9	3		30-34.9	4		
BMI	35-39.9	5		≥40	6		

Smoking | Y | 1 | | N | 2 |

Alcohol use | Y | 1 | | N | 2 |

Physical activity | Y | 1 | | N | 2 |

Carotid stenosis >70% | Y | 1 | | N | 2 |

Not applicable | 9 |

Seizures | Y | 1 | | N | 2 |

Hemorrhagic transformation of infarct | Y | 1 | | N | 2 |

Not applicable | 9 |

Aspirin | Before admission | 1 | | After admission | 2 |

Never | 3 | | Before & after | 4 |

Clopidogrel | Before admission | 1 | | After admission | 2 |

Never | 3 | | Before & after | 4 |

LMW heparin | Before admission | 1 | | After admission | 2 |

Never | 3 | | Before & after | 4 |

Regular heparin | Before admission | 1 | | After admission | 2 |

Never | 3 | | Before & after | 4 |

Warfarin

Before & after 4

Mannitol

Before & after 4

Glycerol

Before & after 4

Statin

Before & after admission 4

Ramipril

Before & after admission 4

Infections during hospitalization

Barthel index admission

Barthel index discharge

Glasgow outcome score admission

Glasgow outcome score discharge

Modified Rankin scale admission

Modified Rankin scale discharge

HbA1C

During admission Insulin used

Type of Insulin – Regular

Type of Insulin – Mixtard

Type of Insulin – NPH

Type of Insulin – Lantus

Type of Insulin – combination (Mention)

Oral hypoclycemia drugs

Hypoglycemia Episodes

BP at admission – diastolic

BP at admission – systolic

Mean arterial pressure

RBC Count

Mean Red Cell Volume

WBC Count

Platelet count

Mean Platelet Volume

MEAN PLATELET VOLUME IN STROKE – CONTROL STUDY

Sl . No.

Hospital No. Lab No.

Name : Age :

Gender : | M | 1 | | F | 2 | |

Weight : Height : BMI:

Hypertension :

Diabetes: | | | | | | |

Total Cholesterol :

HDL :

LDL :

Triglyceride:

Total Cholesterol : HDL ratio :

Recent Myocardial infarction : | | | | | | |

Valvular Heart Disease : | | | | | | |

Atrial Fibrillation : | | | | | | |

Smoking : | | | | | | |

Alcohol Use : | | | | | | |

Physical Activity : | | | | | | |

Previous History of: | | | | | | |

Drug Intake:

RBC Count :

MCV :

WBC Count :

Platelet Count :

Mean Platelet Volume :

GLASGOW OUTCOME SCORE

	Description
5	Good recovery : resumption of normal life despite minor deficits
4	Moderate disability (disabled but independent) : travel by public transportation; can work in sheltered setting
3	Severe disability (conscious but disabled): dependent for daily living.
2	Persistent vegetative state: unresponsive and speechless. After 2-3 weeks may open eyes and have sleep – wake cycles.
1	Death

MODIFIED RANKIN SCALE

	Description
0	No symptoms at all
1	No significant disability despite symptoms: able to carry out all usual duties and activities.
2	Slight disability: Unable to carry out all previous activities but able to look after own affairs without assistance.
3	Moderate disability : requiring some help but able to walk without assistance
4	Moderate disability: unable to walk without assistance and unable to attend to own bodily needs without assistance.
5	Severe disability : bedridden, incontinent and requiring constant nursing care
6	Death

MASTER CHART - MEAN PLATELET VOLUME IN STROKE - CONTROL STUDY

S.No	Age in years	Sex	Weight in kgs	Height incms	Body mass index	Hypertension	Diabetic	Total cholesterol	HDL	LDL	Triglyceride	Total cholesterol : HDL ratio	Recent Mycardical infaction	Valuvar heart disease	Atrial Fibrillation	Smoking	Alchol use	Physical activity	Previous H/O Drug intake	RBC Count in Million/ cumm	MCV (fl)	WBC count in cumm	Platelet count lakhs in cumm	Mean platelet volume (fl)
1	34	1	97	174	32.1	2	2	151	38	103	64	3.9	2	2	2	2	2	1	2	5.5	83	9400	2.4	8.6
2	50	1	74	166	26.9	2	2	196	48	110	92	4.1	2	2	2	2	2	1	2	4.8	84	8300	2.7	7.4
3	47	1	64	164	23.8	2	2	179	34	128	91	5.2	2	2	2	2	2	1	2	5	87	9300	3.1	7.3
4	67	1	71	170	24.5	2	2	157	32	111	73	4.9	2	2	2	2	2	1	2	5	85	9300	1.9	8.6
5	58	2	46	156	18.9	2	2	146	53	70	78	2.8	2	2	2	2	2	1	2	4.4	81	5700	2.8	8.8
6	39	2	56	160	21.8	2	2	141	42	72	116	3.3	2	2	2	2	2	1	2	3.9	90	6800	2.8	7
7	45	1	57	168	20.2	2	2	197	45	128	100	4.3	2	2	2	2	2	1	2	4.8	88	8300	2.9	7.2
8	40	2	58	160	22.7	2	2	201	45	135	96	4.5	2	2	2	2	2	1	2	4.8	85	8300	2.4	7.4
9	54	1	83	168	29.4	2	2	170	32	120	70	5.4	2	2	2	2	2	1	2	5.8	81	6300	1.6	8.7
10	50	2	73	165	26.8	2	2	152	51	84	70	3	2	2	2	2	2	1	2	4.2	83	5300	2.5	8.2
11	47	1	54	160	21	2	2	179	37	120	105	4.5	2	2	2	2	2	1	2	5.4	84	5000	2.4	7.4
12	49	1	53	170	18.3	2	2	103	37	54	76	3.3	2	2	2	2	2	1	2	3.8	53	7800	5.5	7.9
13	26	1	68	170	23.5	2	2	169	45	114	72	3.7	2	2	2	2	2	1	2	5.5	83	7900	2.1	8.1
14	45	1	68	162	26	2	2	177	52	105	87	3.4	2	2	2	2	2	1	2	4.6	89	5200	2.1	7.7
15	33	2	76	158	30.5	2	2	199	34	136	187	5.9	2	2	2	2	2	1	2	4.2	87	9000	3	7.6
16	27	1	62	165	22.8	2	2	121	38	64	82	3.2	2	2	2	2	2	1	2	5	79	6500	2.2	7.9
17	33	1	96	180	29.6	2	2	121	36	64	123	3.5	2	2	2	2	2	1	2	5	87	6400	3.2	8.1
18	31	1	74	174	24.5	2	2	171	40	113	115	4.3	2	2	2	2	2	1	2	5.4	84	6900	2.4	7.4
19	49	2	72	162	27.4	2	2	156	35	101	108	4.5	2	2	2	2	2	1	2	4.3	57	7400	3	8.2
20	26	1	72	176	23.3	2	2	143	34	96	75	4.2	2	2	2	2	2	1	2	5.7	84	6700	3	7.7
21	25	1	59	178	18.7	2	2	137	29	95	101	4.7	2	2	2	2	2	1	2	5.1	82	5800	3.1	7.9
22	53	2	72	164	26.8	2	2	182	87	104	76	3.2	2	2	2	2	2	1	2	3.9	90	4800	2.6	8.3
23	30	1	50	174	16.6	2	2	133	34	80	60	3.9	2	2	2	2	2	1	2	5.2	88	5600	2.8	6.9
24	32	2	67	158	26.9	2	2	182	39	122	88	4.6	2	2	2	2	2	1	2	3.5	90	7000	3.3	8.1
25	36	1	65	168	23	2	2	179	35	120	94	5.1	2	2	2	2	2	1	2	4.7	83	4400	2.2	7.8

S.No	Age in years	Sex	Weight in kgs	Height incms	Body mass index	Hypertension	Diabetic	Total cholesterol	HDL	LDL	Triglyceride	Total cholesterol : HDL ratio	Mycardical infaction	Valuvar heart disease	Atrial Fibrillation	Smoking	Alchol use	Physical activity	Previous H/O Drug intake	RBC Count in Million/ cumm	MCV (fl)	WBC count in cumm	Platelet count lakhs in cumm	Mean platelet volume (fl)
26	26	1	62	166	22.5	2	2	163	34	113	172	4.8	2	2	2	2	2	1	2	5	89	6300	2.8	7
27	21	1	53	172	17.9	2	2	153	40	97	70	3.9	2	2	2	2	2	1	2	4.6	91	5700	3.2	6.9
28	31	1	65	174	21.5	2	2	163	38	103	79	4.3	2	2	2	2	2	1	2	5.2	81	7300	2.3	8.1
29	31	2	51	164	19	2	2	150	37	103	70	4	2	2	2	2	2	1	2	4.5	88	5400	2.7	7.7
30	36	1	76	176	24.6	2	2	140	36	86	61	3.8	2	2	2	2	2	1	2	4.8	85	7100	3.7	7.4
31	58	1	75	170	26	2	2	174	38	107	117	4.6	2	2	2	2	2	1	2	4.9	76	8400	3.3	7.9
32	56	1	74	176	24	2	2	156	37	104	71	4.2	2	2	2	2	2	1	2	4.8	87	6300	2.8	7
33	30	2	59	158	23.6	2	2	140	45	83	61	3.1	2	2	2	2	2	1	2	4.2	66	5800	3.3	7
34	34	2	75	156	30	2	2	194	52	127	84	3.7	2	2	2	2	2	1	2	5	77	9000	3.8	7.7
35	33	1	87	166	31.6	2	2	158	38	112	78	4.1	2	2	2	2	2	1	2	5.2	88	7700	3.1	7.6
36	25	2	75	175	24.6	2	2	182	54	113	100	3.4	2	2	2	2	2	1	2	5	88	6600	3	7.2
37	44	2	70	172	23.7	2	2	154	50	93	82	3.1	2	2	2	2	2	1	2	5.5	84	8400	2.5	7.9
38	36	2	65	152	28.1	2	2	122	30	75	93	4.1	2	2	2	2	2	1	2	4.1	83	7700	3.6	6.4
39	51	1	63	162	24	2	2	184	61	95	72	3	2	2	2	2	2	1	2	4.7	82	9100	3.9	7.6
40	37	2	85	160	33.2	2	2	171	34	121	60	5	2	2	2	2	2	1	2	4.5	75	9300	3.6	7.9
41	40	2	59	154	24.8	2	2	178	38	113	95	4.6	2	2	2	2	2	1	2	4.3	86	6800	2.4	8.1
42	38	2	65	154	27.4	2	2	152	27	96	131	5.5	2	2	2	2	2	1	2	4.5	82	6100	3.1	7.7
43	41	1	58	165	21.3	2	2	114	30	73	101	3.8	2	2	2	2	2	1	2	6	76	9600	3	7.4
44	50	1	64	164	23.8	2	2	140	35	90	70	4	2	2	2	2	2	1	2	4.9	92	7000	2.2	7.2
45	42	2	54	158	21.6	2	2	203	43	136	156	4.7	2	2	2	2	2	1	2	4.6	83	9300	2.9	6.9
46	55	1	54	160	21	2	2	184	39	118	163	4.7	2	2	2	2	2	1	2	5	85	9800	3.3	7.2
47	29	1	72	187	20	2	2	184	46	114	98	4	2	2	2	2	2	1	2	4.6	86	5500	2.3	7.7
48	45	2	58	156	23.8	2	2	221	46	141	94	4.8	2	2	2	2	2	1	2	4.3	87	7700	3.8	6.8
49	32	2	54	156	22.2	2	2	158	40	106	72	4	2	2	2	2	2	1	2	4.3	83	7500	2.9	7.3
50	54	1	65	174	21.5	2	2	139	30	93	114	4.6	2	2	2	2	2	1	2	5.3	84	8600	2.5	7

MASTER CHART - MEAN PLATELET VOLUME IN STROKE - CASE STUDY

S.No	Agein years	Sex	Type of stroke	Territory (Ischemic)	Region (Hemorrhage)	Hemisphere	Recurrence of stroke	Duration in minutes Onset of stroke – 1st medical	Duration in minutes to reach territory hospitals	Reason for dely	Distance from Territory hospital	Door to CT/MRI (minutes)	Door to Aspirin / Clopidrogel (minutes)	Hypertension	Duration of year Hypertension (months)	Diabetes	Duration of year diabetic (months)	Total cholestsl	HDL	LDL	Triglycerine	Total Cholesterol/HDL ratio	Recent myocardial infarction	Valvular Heart Disease	Atrial Fibrillation	Weight in Kg	Height in Cm	Body Mass Index	Smoking	Alcohol Abuse	Physical Activity	Carotid Steosis >70%	Seizures	Hge Transformatin of Infarct	Aspirin	Ciopidogrel	LMW Heparis
1	53	1	1	5	9	2	2	30	2220	1	130	2520	3120	1	24	1	24	160	46	92	330	3.5	2	2	2	65	174	21.5	2	1	1	1	2	2	2	2	3
2	57	1	1	1	9	1	2	10	210	1	100	220	400	2	-	1	300	158	30	112	51	5.2	2	2	2	59	160	23.5	2	2	1	2	2	2	3	2	2
3	51	1	1	5	9	3	1	15	1080	1	60	1200	1455	1	144	2	-	121	34	72	54	3.6	2	2	2	-	-	-	1	1	1	2	2	2	4	4	3
4	57	1	1	4	9	1	1	90	180	1	18	120	150	1	180	1	180	169	33	113	110	5.1	1	2	2	55	161	21.2	2	2	1	3	2	2	2	2	3
5	58	1	2	9	1	1	2	15	160	2	100	150	-	1	36	1	120	213	34	130	265	6.2	2	2	2	-	-	-	1	1	1	9	2	9	3	3	3
6	52	1	1	1	9	2	2	90	360	1	20	380	500	2	-	2	-	196	47	128	110	4.2	2	2	2	-	-	-	1	1	1	2	2	2	2	3	2
7	88	2	1	1	9	1	2	360	540	1	30	570	750	2	-	2	-	159	38	98	101	4.2	2	2	2	-	-	-	2	2	1	3	2	2	3	2	3
8	46	1	1	1	9	2	2	90	1200	1	150	180	210	2	-	2	-	246	36	190	283	6.8	2	2	2	-	-	-	2	1	1	2	2	2	3	2	3
9	40	1	2	9	1	1	2	30	1440	1	5	60	-	2	-	2	-	173	35	118	169	4.9	2	2	2	-	-	-	2	2	1	9	2	9	3	3	3
10	43	1	1	5	9	2	2	30	30	2	10	45	120	1	-	2	-	204	32	151	139	6.3	2	2	2	-	-	-	1	1	1	2	2	2	2	3	3
11	39	1	1	1	9	2	2	30	1440	1	2	120	180	2	-	2	-	151	51	78	73	3	2	2	2	80	160	31.25	2	2	1	2	2	2	2	3	3
12	58	1	1	1	9	1	2	30	720	3	140	750	775	2	-	2	-	248	36	189	130	6.8	2	2	2	-	-	-	2	1	1	3	2	2	2	3	3
13	65	1	1	1	9	2	2	30	480	1	150	510	570	1	120	2	-	193	40	110	79	4.8	2	2	2	-	-	-	2	2	1	3	2	2	3	2	3
14	41	2	1	1	9	1	2	30	2880	1	3	60	90	1	36	1	36	156	38	84	108	4.1	2	2	2	-	-	-	2	2	2	2	2	2	4	3	3
15	35	1	2	9	3	1	2	60	1440	1	100	180	-	2	-	2	-	163	40	110	88	4	2	2	2	65	176	21	1	1	1	9	2	9	3	3	3
16	70	2	1	1	9	2	2	30	30	2	10	40	180	1	18	1	24	208	38	156	133	5.4	2	2	2	-	-	-	2	2	2	2	2	1	2	2	2
17	57	1	1	4	9	2	2	30	2880	1	15	75	120	1	120	2	-	179	39	111	118	5.1	2	2	2	82	170	28.3	2	2	1	2	2	2	2	3	3
18	51	1	1	1	9	2	2	15	2880	1	150	45	60	1	120	2	-	348	48	244	193	7.3	2	2	2	79	170	27.3	1	1	1	3	2	2	4	3	3
19	60	1	1	1	9	2	1	60	1440	1	80	120	180	1	120	2	-	133	31	78	132	4.3	2	2	2	-	-	-	2	2	1	1	1	2	4	4	1
20	45	1	1	1	9	1	2	360	610	1	100	390	650	1	24	2	-	199	41	136	123	4.8	2	2	2	56	160	21.8	2	2	1	2	2	2	2	2	3
21	53	1	1	1	9	2	2	60	2880	1	100	75	95	1	6	2	-	100	28	49	172	3.6	1	2	2	65	162	24.8	1	2	1	2	2	2	4	4	1
22	64	1	1	4	9	3	2	60	60	2	25	75	90	2	-	2	-	201	43	129	93	4.7	2	2	2	-	-	-	2	2	1	3	2	2	3	2	2
23	70	2	1	4	9	3	1	15	900	1	80	240	960	2	-	2	-	172	60	85	46	2.9	2	2	2	-	-	-	2	2	1	2	2	2	2	3	2
24	44	2	1	9	9	2	2	30	240	1	140	280	-	2	-	2	-	97	25	65	91	3.7	2	2	2	40	150	17.1	2	2	1	9	2	1	3	3	2
25	68	1	2	9	3	2	1	30	180	1	92	210	-	1	36	2	-	229	62	135	157	3.7	2	2	2	65	162	24.8	2	2	1	9	2	1	1	1	3
26	65	1	1	1	9	2	2	2880	2880	2	200	2910	2940	2	-	2	-	222	35	168	139	6.4	2	2	2	50	155	20.8	2	2	1	2	2	2	2	2	2

27	68	1	1	1	9	2	2	60	80	1	10	90	110	2	-	2	-	140	32	82	166	4.4	2	2	2	57	155	23.75	2	2	1	2	2	2	4	1	3
28	52	1	1	4	9	3	2	30	2880	1	10	2910	2950	2	-	1	12	184	34	132	78	5.4	2	2	2	64	170	22.1	2	1	1	2	2	2	3	2	3
29	35	2	1	1	9	1	2	60	300	1	140	90	330	2	-	1	6	196	32	126	76	6.1	2	2	2	75	159	29.76	2	2	1	2	2	2	3	2	3
30	56	1	2	9	1	2	2	60	720	1	80	750	-	1	24	1	84	222	35	168	150	6.3	2	2	2	-	-	-	1	1	1	9	2	9	3	3	3
31	55	2	1	4	9	3	2	120	4320	1	90	500	550	2	-	2	-	135	35	86	78	3.9	2	2	2	55	160	21.48	2	2	1	3	2	2	2	3	3
32	60	2	1	1	9	2	2	120	180	1	80	200	220	1	1	2	-	169	34	109	114	4.9	2	2	2	57	155	23.75	2	2	1	3	2	2	2	2	3
33	60	1	2	9	3	2	2	30	250	1	40	240	-	2	-	2	-	230	38	110	78	6.1	2	2	2	-	-	-	1	2	1	9	2	9	3	3	3
34	76	1	1	2	9	2	2	30	720	1	15	750	780	1	3	1	3	180	40	127	105	4.5	1	2	2	-	-	-	2	2	1	2	2	2	2	2	3
35	70	1	1	1	9	1	2	30	90	1	5	110	140	2	-	1	60	140	42	130	110	3.3	2	1	2	-	-	-	1	1	1	3	2	2	3	2	3
36	48	1	1	1	9	2	2	60	180	1	100	400	430	1	1	1	1	151	44	87	70	3.4	2	2	2	52	160	20.3	2	2	1	2	2	2	1	4	3
37	68	1	2	9	6	2	2	30	120	1	70	150	-	1	72	2	-	195	40	104	202	4.8	2	2	2	-	-	-	1	1	1	9	2	9	3	3	3
38	49	1	1	1	9	2	2	30	2160	1	90	240	280	2	-	2	-	155	32	102	130	4.8	2	2	2	-	-	-	2	2	1	3	2	2	3	2	1
39	71	1	2	9	1	2	1	30	270	1	180	300	-	1	48	1	240	107	40	110	105	2.6	2	2	2	-	-	-	2	2	1	9	2	1	1	3	3
40	60	1	1	5	9	2	1	30	2880	1	10	120	180	1	120	1	120	86	32	40	114	2.7	2	2	2	-	-	-	2	1	1	2	2	2	1	4	3
41	47	1	1	2	9	2	2	60	90	1	20	120	180	1	12	2	-	132	31	84	94	4.3	2	2	2	-	-	-	2	2	1	2	2	2	2	3	3
42	54	1	1	1	9	1	2	45	45	2	15	90	120	1	48	2	-	272	42	188	169	6.4	2	2	2	72	170	24.9	1	1	1	2	2	2	3	2	3
43	70	1	1	1	9	2	2	2880	3000	3	45	2940	3020	1	4	1	180	181	30	109	212	6	2	2	2	60	160	23.43	2	2	1	2	2	2	1	2	3
44	51	2	1	1	9	1	2	30	1560	1	10	100	150	2	-	1	72	125	23	80	143	5.6	2	2	2	51	151	22.36	2	2	1	2	2	2	3	2	3
45	30	1	1	1	9	1	2	360	4320	1	15	480	-	2	-	2	-	200	40	100	75	5	2	2	2	40	155	16	1	1	1	3	2	2	3	3	3
46	50	1	1	1	9	1	2	30	2880	1	150	200	250	1	120	1	204	176	40	110	196	4.4	2	2	2	-	-	-	1	1	1	3	2	2	1	1	3
47	51	1	1	4	9	2	2	45	2880	1	200	240	300	1	60	1	132	134	30	78	113	4.4	2	2	2	56	153	23.93	2	2	1	3	2	2	4	4	3
48	65	1	2	9	1	1	2	35	90	1	30	140	-	1	36	2	-	140	42	90	110	3.3	2	2	2	-	-	-	2	1	1	9	2	9	3	3	3
49	77	1	1	1	9	2	2	30	60	1	10	75	120	2	-	2	-	115	35	70	51	3.3	2	2	2	65	160	25.39	2	2	1	2	2	2	3	2	3
50	84	1	1	1	9	1	2	45	1440	1	50	1400	1500	2	-	1	120	147	28	96	80	5.2	1	2	2	-	-	-	1	1	1	2	2	2	2	2	3

Regular Heparin	Warfarin	Mannitol	Glycerol	Statin	Ramipril	Infetion during Hospitalization	Barmel - Index Admission out of 100	Barmel Index Discharge out of 100	Glasgow outcome score Admission	Glasgow outcome score Discharge	Mod Ranking scale Admission	Mod Ranking scale Discharge	HbA1c%	Insulin used during admission	Regular Insulin	Mixtard Insulin	NPH Insulin	Lantus	Combnation Insulin	Oral Hypoglycemic Drug	Hypoglycemic Episode	Diastolic BP on Admission	Systolic BP on Admission	Mean Arterial Pressure	RBC count in million	Mean corruscular volume (fL)	WBC count in cumm	Platelet count in lakhs	Mean platelet volume (fL)
3	3	3	3	2	2	2	40	80	3	4	4	3	14.3	1	1	1	2	2	1	1	2	80	130	96.6	4.1	91	6300	1.5	8.6
3	3	2	3	2	2	2	-	55	3	4	5	4	12	1	1	1	2	2	1	2	2	70	150	96.6	4.4	80	13600	3	6.5
2	3	3	3	2	2	1	-	45	3	4	4	4	-	2	2	2	2	2	2	2	2	90	120	100	4.3	91	10700	2.2	7.7
3	3	3	3	2	2	2	50	75	3	5	4	3	9.2	1	1	1	2	2	1	1	2	100	190	130	4.5	84	13300	2.2	7.4
3	3	4	2	3	2	1	-	50	3	3	4	4	14.7	1	1	2	2	2	2	1	2	110	210	143.3	4.2	83	10000	1.6	7.6
2	2	2	2	2	2	1	-	40	3	3	5	4	-	2	2	2	2	2	2	2	2	90	140	106.6	4.2	100	9100	2.6	7
3	3	3	3	2	2	1	25	40	3	3	4	4	-	2	2	2	2	2	2	2	2	80	160	106.6	3.9	86	8800	2.4	8.1
3	3	3	3	2	2	2	50	50	3	3	3	3	-	2	2	2	2	2	2	2	2	110	140	120	4.8	92	9000	2.3	8.4
3	3	4	4	3	2	2	50	65	3	4	4	4	-	2	2	2	2	2	2	2	2	130	190	150	5.8	82	20700	2.5	9.2
3	3	3	3	2	2	2	85	100	4	5	5	2	-	2	2	2	2	2	2	2	2	110	220	143.3	4.6	93	5700	1.8	7.3
3	3	2	2	2	2	1	-	100	3	5	5	0	-	2	2	2	2	2	2	2	2	90	140	106.6	4.7	83	14400	2	7.6
3	3	2	2	2	2	2	-	-	3	3	4	4	-	2	2	2	2	2	2	2	2	110	150	123.3	4.5	91	7500	1.4	7.2
3	3	3	3	2	2	2	-	-	3	3	4	4	-	2	2	2	2	2	2	2	2	80	110	90	4.1	83	14800	3.4	7.9
3	3	3	3	2	2	2	-	50	3	3	4	4	10	1	1	1	2	2	1	1	2	100	150	116.6	3	87	8900	1.8	7.7
3	3	3	3	3	2	1	5	85	3	5	5	2	-	2	2	2	2	2	2	2	2	100	170	123	5.2	88	12200	2.3	9.6
3	2	3	3	2	2	1	-	15	3	3	5	4	11	1	1	1	2	2	1	2	2	100	140	113.3	4.5	82	8500	2	7.3
3	3	3	3	2	2	1	25	75	3	5	4	3	-	2	2	2	2	2	2	2	2	110	190	136.6	4.3	86	10800	3.5	7.9
3	3	3	3	4	2	2	70	90	5	5	3	2	-	2	2	2	2	2	2	2	2	110	180	133.3	4.4	86	9900	3.4	7
1	3	3	3	2	2	1	30	30	3	4	4	4	-	2	2	2	2	2	2	2	2	70	110	113.3	4.8	86	6300	1.8	9.2
3	2	3	3	2	2	2	20	75	3	4	5	3	-	2	2	2	2	2	2	2	2	90	150	110	5.5	74	11200	2.1	7
3	3	3	3	4	2	2	25	40	4	5	4	3	-	2	2	2	2	2	2	2	2	90	120	100	4.9	82	16400	3.2	7.3
2	2	3	2	2	2	1	-	20	3	4	5	4	12.6	1	1	1	2	2	1	2	2	100	160	120	4.4	85	7800	1.6	8.4
3	3	3	3	2	3	2	-	60	4	4	5	5	-	2	2	2	2	2	2	2	2	90	150	110	3.8	90	18800	3.4	6.7
3	2	4	3	3	3	1	-	60	2	4	5	3	8	2	2	2	2	2	2	2	2	100	140	113.3	4.6	54	4200	3.1	7.4
3	3	3	3	4	1	2	85	95	4	5	2	1	8.7	2	2	2	2	2	2	2	2	100	170	123	4.3	85	8500	2.3	6.9
3	2	3	3	2	2	2	45	65	3	4	5	4	-	2	2	2	2	2	2	2	2	100	150	116.6	4.4	83	6800	2.97	7.2

3	3	3	3	2	2	2	40	85	4	5	4	3	-	2	2	2	2	2	2	2	2	120	220	153.3	5	83	6800	2.73	6.8
3	3	3	3	2	3	2	85	95	4	5	2	1	5.7	1	1	2	2	2	2	1	2	110	200	140	4.9	84	9000	3.1	8.1
3	3	3	3	2	2	2	40	85	4	5	4	3	7.5	2	2	2	2	2	2	1	2	100	180	126.6	4.8	71	12500	2.7	8.3
3	3	2	2	2	2	1	-	10	3	3	4	4	-	1	1	1	2	2	1	2	2	100	160	120	4.5	79	9000	3.7	8.6
3	3	2	3	2	2	2	-	80	3	4	5	2	-	2	2	2	2	2	2	2	2	80	130	146.6	4.9	83	21700	3	8.1
3	3	3	3	2	2	2	45	60	4	4	4	4	-	2	2	2	2	2	2	2	2	90	140	106.4	3.8	92	9100	3.4	6.9
3	3	2	3	3	2	1	-	40	3	3	5	4	-	2	2	2	2	2	2	2	2	120	230	156.6	3.2	73	7100	2	9.6
2	3	3	3	2	2	2	50	70	3	4	4	3	-	1	1	2	2	2	2	1	2	90	150	110	5.2	84	8400	2.2	8.3
2	2	3	3	2	3	1	45	60	4	4	4	4	-	1	1	2	2	2	2	2	1	70	100	80	4.7	77	8200	3.1	8.2
3	3	3	3	4	2	2	90	95	4	4	1	1	4.5	2	2	2	2	2	2	2	2	110	150	130	5.1	88	7900	2.26	8.1
3	3	2	3	3	3	1	-	45	2	4	5	3	-	2	2	2	2	2	2	2	2	96	150	106	5.2	86	14500	2.5	7.9
3	3	4	4	2	2	1	-	20	2	3	3	4	-	2	2	2	2	2	2	2	2	100	150	116.6	5.1	57	16600	3.7	8.1
3	3	2	3	4	4	2	-	10	2	2	4	4	-	2	2	2	2	2	2	2	2	80	200	120	4.3	89	12900	2.1	6.5
1	1	1	1	4	2	2	5	40	3	3	5	4	6.6	1	1	2	2	2	2	2	1	80	150	103.3	4.3	74	8000	2.4	8.3
3	3	3	3	2	2	1	15	30	3	3	4	4	-	2	2	2	2	2	2	2	2	90	190	123.3	4.7	85	10900	2.3	7.8
3	3	3	3	2	2	2	35	95	4	5	4	1	-	2	2	2	2	2	2	2	2	160	260	193.3	5.7	87	6800	2.5	9
3	3	3	3	4	2	2	40	10	4	3	4	5	5.8	1	1	2	2	2	2	2	2	120	160	133.3	5.5	81	12200	2.6	7.2
3	3	3	3	2	2	2	85	95	5	4	2	1	7.4	1	1	2	2	2	2	1	2	80	130	96.6	3.6	86	7800	2.7	6.8
3	3	2	3	3	3	1	10	20	3	3	4	4	-	2	2	2	2	2	2	2	2	80	140	100	3.4	98	6700	1.6	8.3
3	3	4	3	1	2	2	-	10	2	2	5	5	-	1	1	2	2	2	2	2	2	70	90	77	6.5	82	19300	2.5	8.8
3	3	3	3	2	2	2	95	100	4	5	3	2	-	2	2	2	2	2	2	2	2	90	180	120	3.6	86	8900	2.9	7
3	3	2	2	3	3	2	-	5	2	2	5	5	-	2	2	2	2	2	2	2	2	110	230	150	5.3	82	30100	2.8	8.4
3	3	3	3	2	2	2	85	85	4	4	2	2	-	2	2	2	2	2	2	2	2	90	140	106	4.9	88	7400	2.5	7.3
2	3	3	3	2	2	1	-	30	4	4	4	4	6.3	2	2	2	2	2	2	1	2	100	170	123	3.8	91	9500	2.2	8.2

K. Dis.No.10498/E4/1/2006.

Govt. Rajaji Hospital,
Madurai – 625 020. Dt. 07.07.06.

Sub: Establishment – Govt. Rajaji Hospital, Madurai – Ethical Committee Projects approved by the Committee – Intimation – Sent – Reg.

The Ethical Committee of the Govt. Rajaji Hospital, Madurai was held at 12.30 pm. on 07.07.2006 at the Dean's Chamber, Govt. Rajaji Hospital, Madurai, and the following Projects were approved unanimously by the Committee Members.

S.No.	Name of the Student	Name of the Project approved
01)	Dr. G. Nagasundar, PG in M.D.General Medicine.	"Mean Platelet volume in Cerebro-vascular Accidents"
02)	Dr. Harihara Krishnan, PG in M.D.General Medicine.	"Pseudochloinesterase level in Organo Phosporous Poisoning"
03)	Dr.P. Abeesh, PG in M.D.General Medicine.	"Homocysteine level in Coronary Artery Disease patients"
04)	Dr. A. Vinodhkumar Adithyaa, MBBS Student (Prefinal) Madurai Medical College.	Nasal carriage of Methicillin – Resistant Staphylococcus Aureus among Surgery Unit Staff and patients.(ICMR scheme)
05)	Dr. M.L.Vasanthakumari,MD,DCH, Professor & HOD of Paediatric Medicine.	"Evaluate the RNTCP diagnostic algorithm for Paediatric Pulmonary TB"
06)	Dr.C. indira Priyadarshini,MD, Director,Instt, of Microbiology, Madurai Medical College,	Gene sequencing of metronidazole resistant bacteroides fragilis.
07)	Dr.M. Srinivasan, MMBS Student (Prefinals) Madurai Medical College.	Intestinal Parasitoses and Salmonella Carrier State Among Prisoners in Madurai.
08)	Dr. Lavanya, PG in Microbiology, Madurai Medical College	Gene Sequencing of Vancomycin resistant enterococci.

Please note that the investigator should adhere the following:-

01) She/He should get a detailed informed consent from the patients/participants and maintain confidentially.
02) She/He should carry out the work without detrimental to regular activities as well as without extra expenditure to the Institution or Government.
03) She/He should inform the Institution Ethical Committee in case of any change of study procedure site and investigation or guide.
04) She/He should not deviate for the area of the work for which applied for Ethical clearance.
05) She/He should inform the IEC immediately, in case of any adverse events or serious adverse reactions.
06) She/He should abide to the rules and regulations of the Institution.
07) She/He should complete the work within the specific period and apply for, if any extension of time is required, She should apply for permission again and do the work.
08) She/He should submit the summary of the work to the Ethical Committee on completion of the work.
09) She/He should not claim any funds from the Institution while doing the work or on completion.
10) She/He should understand that the members of IEC have the right to monitor the work with prior intimation.

13/7

Dean/Chairman,
Ethical Committee, Govt. Rajaji Hospital, Madurai.

To As Above

13/7 Forwarded: H.O.D.